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☐	L11	L9 and bioswitch	1
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☐	L9	L8 and mammal	179
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☐	L4	L3 and electrode	2259
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☐	L1	metal antibody conjugate	4368854

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DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=OR			
L26	L21 and electrode	5	L26
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L18	L17 and electrical	34	L18
L17	L16 and specific	178	L17
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L15	L14 and bound	178	L15
L14	L13 and antigen	178	L14
L13	L9 and detect	178	L13

L12	L9 and lebrun	1	L12
L11	L9 and bioswitch	1	L11
L10	L9 and bioswich	0	L10
L9	L8 and mammal	179	L9
L8	L7 and spot	192	L8
L7	L6 and autoimmune	421	L7
L6	L4 and immobiliz?	653	L6
L5	L4 and immobliz?	0	L5
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L3	L2 and IgG	26246	L3
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L1	metal antibody conjugate	4368854	L1

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1: CRC Crit Rev Clin Lab Sci. 1980;12(2):123-70. Related Articles

Soluble immune complexes in human disease.

Nydegger UE, Davis JS 4th.

The great variety in biochemical properties of immune complexes occurring human and animal disease states has made the detection of such complexes a difficult task. Variability in immune complex size, specificity, and interactio with humoral or cellular receptor systems, such as complement and phagocyt suggests different pathogenic properties. The introduction of radioimmunoas and the recently improved knowledge of the immune complex-receptor interactions have lead to the description of a large number of detection procedures, which in turn has widened the catalogue of diseases associated w immune complexes. This widespread occurrence of soluble immune complex has lead many investigators to think that such complexes may occur either as transient physiological phenomenon, important for fast clearance of the antig as primary pathogenic factors triggering inflammatory reactions. Among the procedures for immune complex detection known today, the article will selec some pertinent tests, which will be discussed with respect to their specificity, sensitivity, and reproducibility. Furthermore, it is well known that when appl the study of a patient group with one particular immune complex disease, vai tests will result in different percentages of patients having complexes. This observation is due to differences in the underlying principle on which the vai tests are based. Thus immune complexes must be further characterized with respect to their size, to the antibody class or specificity involved and, most difficult, to the antigenic specificity which participates in the complex. Recei advances in such experimental characterization of immune complexes in vitr in the clinical evaluation of patients with complement activation associated t presence of immune complexes will be discussed.

Publication Types:
- Review

PMID: 6446444 [PubMed - indexed for MEDLINE]

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Mar 3 2005 14:57:42

1: J Nephrol. 2002 Nov-Dec;15 Suppl 6:S20-7.

JOnline

The use of laboratory tests in diagnosis and monitoring of systemic lupus erythematosus.

Sinico RA, Bollini B, Sabadini E, Di Toma L, Radice A.

Nephrology and Dialysis Unit and Center of Clinical Immunology and Rheumatology, San Carlo Borromeo Hospital, Milan, Italy. renato.sinico@oscb.sined.net

Clinical immunology laboratories play an essential role in diagnosis and monitoring of systemic lupus erythematosus (SLE). To obtain the best results in terms of diagnostic performance and clinical usefulness, the following recommendations should be fulfilled: Indirect immunofluorescence on Hep-2 cells remains the method of choice for the detection of anti-nuclear antibodies (ANA). The sensitivity of ANA test for SLE is very high (almost 100%) but its specificity low since ANA can be present in a number of different clinical conditions and even in normal controls. Anti-dsDNA antibodies are highly specific for SLE and present in a high proportion of SLE patients (40-80%). The method of choice for anti-ds DNA is the Farr assay; however, the necessity of using radioactive material decreases its applicability. As an alternative, immunofluorescence on Crithidia Luciliae can be used in the diagnostic phase for its high specificity. It is not advisable to use ELISA, in the diagnostic phase, due to its low specificity. The quantitative determination of anti-dsDNA is useful for monitoring patients, in particular in the presence of nephritis. For monitoring, a quantitative method should be used (Farr assay or ELISA). The detection of antibodies to extractable nuclear antigens (ENA) and to phospholipids (Lupus anticoagulant and anti-cardiolipin antibodies with a beta2 glycoprotein I-dependent method) are useful to identify subgroups of patients at risk for some clinical manifestations (i.e. anti-phospholipid syndrome). New assays (anti-C1q and anti-nucleosome antibodies) have been recently proposed for diagnosis (anti-nucleosome) and

monitoring SLE patients (anti-C1q and anti-nucleosome antibodies), with promising results. Among biological parameters, urinary levels of monocyte chemoattranct protein 1 (MCP1) seem to be the most useful to monitor nephritis activity in lupus patients.

Publication Types:

- Review
- Review, Tutorial

PMID: 12515370 [PubMed - indexed for MEDLINE]

L2: Entry 5 of 9 File: USPT Jul 12, 1994

US-PAT-NO: 5328847
DOCUMENT-IDENTIFIER: US 5328847 A

TITLE: Thin membrane sensor with biochemical switch

DATE-ISSUED: July 12, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Case; George D.	Aloha	OR	97007	
Worley, III; Jennings F.	Durham	NC	27713	

US-CL-CURRENT: 205/778; 204/403.06, 204/403.08, 422/68.1, 422/69, 435/287.1, 435/287.2, 435/817

CLAIMS:

What is claimed is:

1. An electrochemical biosensor capable of signalling the presence of a target agent, comprising

a. a biochemical switch comprising a hydrophilic film layer containing a recognition biomolecule, the recognition biomolecule having an ion channel blocker and a recognition moiety capable of specifically binding with a target agent,

b. a hydrophobic gate membrane comprised of membrane material and ion channel gate material, in contact with the biochemical switch, and

c. a measuring device comprising a conductive measuring electrode in contact with the gate membrane, and means for measuring a current surge between the biochemical switch and the measuring electrode in response to exposure to a target agent.

2. The biosensor of claim 1 wherein the recognition moiety is selected from the group consisting of an antibody to an antigen target agent, hapten to an antibody target agent, and antigen to an antibody target agent.

3. The biosensor of claim 1 wherein the ion channel blocker is a polyvalent cation.

4. The biosensor of claim 1 wherein the ion channel blocker is ruthenium red.

5. The biosensor of claim 1 wherein the channel blocker is a guanidinium compound and the ion channel is a sodium channel.

6. The biosensor of claim 1 wherein the ion channel blocker is a trivalent lanthanide.

7. The biosensor of claim 6 wherein the lanthanide is selected from the group consisting of dysprosium and gadolinium.

8. The biosensor of claim 1 wherein the recognition moiety is a protein selected from the group consisting of albumin and immunoglobulin.

9. The biosensor of claim 1 wherein the gate membrane is a plastic.

10. The biosensor of claim 1 wherein the gate membrane is a mixture of plastic and lipid.

11. The biosensor of claim 1 wherein the gate membrane comprises a solid layer of a mixture of alcohol, carboxylic acid and aldehyde with about 17 carbon atoms.

12. The biosensor of claim 1 wherein the gate membrane material comprises an acrylic polymer.

13. The biosensor of claim 1 wherein the gate membrane material is selected from the group consisting of polylaurylmethacrylate, carboxylated polyacrylamide, and styrene polyvinylpyridine copolymer.

14. The biosensor of claim 1 wherein the gate membrane material comprises a phospholipid or fatty acid derivative.

15. The biosensor of claim 1 wherein the gate material is selected from the group consisting of channel-forming antibiotics, physiological calcium channels, acetylcholine receptor channels, and physiological sodium channels.

16. The biosensor of claim 1 wherein the gate material is comprised of a gramicidin antibiotic ion channel.

17. The biosensor of claim 1 wherein the measuring device comprises a wheatstone bridge circuit.

18. The biosensor of claim 1 wherein the biochemical switch includes gelatin, the recognition biomolecule is an immunoglobulin-lanthanide conjugate, the gate membrane is a carboxylated acrylic polymer latex with gramicidin ion channels, and the measuring device is a resistance circuit capable of measuring a current surge when the biosensor is exposed to antigen.

19. The biosensor of claim 1 wherein the indicator means is an audible alarm.

20. The biosensor of claim 1 wherein the indicator means is a visible display.

21. The biosensor of claim 1 wherein the measuring device in contact with the gate membrane is constructed so as to be able to be regenerated and used with a variety of biochemical switches.

22. A method of using a biosensor, the method comprising:

providing a biochemical switch having a hydrophilic film layer containing a recognition biomolecule, the recognition biomolecule having an ion channel blocker and a recognition moiety capable of specifically binding with a target agent, a hydrophobic gate membrane containing ion channels in contact with the biochemical switch, and a measuring device, said measuring device comprising a conductive measuring electrode in contact with the gate membrane, and means for measuring a current surge between the biochemical switch and the measuring

electrode,

placing the biosensor in an environment suspected of containing a target material,

contacting the biochemical switch to the suspected environment, and

determining the presence of the target material.

23. A method of making a biosensor, the method comprising:

providing a biochemical switch having a hydrophilic film layer containing a recognition biomolecule, the recognition biomolecule having an ion channel blocker and a recognition moiety capable of specifically binding with a target agent,

providing a hydrophobic gate membrane containing ion channels,

providing a measuring device, said measuring device comprising a conductive measuring electrode and means for measuring a current surge between the biochemical switch and the measuring electrode,

connecting the gate membrane to the measuring device, and

connecting the biochemical switch with the gate membrane.

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L2: Entry 3 of 9 File: USPT Jan 7, 2003

US-PAT-NO: 6503452
DOCUMENT-IDENTIFIER: US 6503452 B1

TITLE: Biosensor arrays and methods

DATE-ISSUED: January 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Boxer; Steven	Stanford	CA		
Kam; Lance	Palo Alto	CA		

US-CL-CURRENT: 422/82.02; 422/82.06, 427/2.13

CLAIMS:

It is claimed:

1. A method for forming an array of biosensor regions, where each region has a different, known lipid bilayer compositions comprising the steps of: providing a biosensor array having a plurality of lipid bilayer compatible regions, each compatible region being surrounded by one or more bilayer barrier regions, providing a gradient forming device loaded with two or more different lipid bilayer compositions, the gradient forming device in fluid communication with a spot forming device for forming spots on a surface, providing a multi-axis translation table for holding and translating a biosensor array workpiece, placing a biosensor array workpiece that has a plurality of bilayer compatible regions surrounded by one or more barrier regions, and forming spots of mixed lipid bilayer compositions resulting from the gradient forming device forming a gradient and translating the table in at least one axis while dispensing such composition mixture as it is formed, thereby dispensing to different, consecutive locations different ratios of each of the lipid bilayer compositions.

2. A method for making gradient biosensor array comprising the steps of: mixing together first and second different lipid bilayer forming compositions contained from first and second sources by flowing in a substantially laminar flow, two different compositions from two different sources into one mixing chamber that substantially retains the laminar flow character of the two different compositions while flowing through the mixing chamber, where the facing edges of each different composition mix to form a gradient having a first edge and a second edge and further comprising composition combinations of different ratios beginning from the first edge of the gradient that faces the first composition, and ending at the second edge of the gradient that faces the other, second composition, and where the mixing chamber is adapted to dispense the gradient in a substantially laminar flow across the surface of the array, and where the compositions contained in the gradient are captured and retained upon initial contact by bilayer-compatible regions of the array.

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L12: Entry 2 of 2 File: PGPB Jul 17, 2003

DOCUMENT-IDENTIFIER: US 20030134299 A1
TITLE: Methods and devices based upon a novel form of nucleic acid duplex on a surface

Classification at Publication, US Primary Class/Subclass:
435/6

Current US Classification, US Primary Class/Subclass:
435/6

Summary of Invention Paragraph:
[0002] Microarray technology has revolutionized applied genomics (Cheung V G et al., 1999, Nature Genetics 21:15-19; Duggan D J et al., 1999, Nature Genetics 21:10-14). It is based upon hybridization of a surface-bound nucleic acid to a nucleic acid in solution to form a Watson-Crick double helix by a mixed phase reaction between complementary nucleic acid strands. The secondary structure of the resulting double helix is determined, in part, by base pairing and base stacking, in conjunction with the constraints imposed on phosphodiester backbone conformation and sugar pucker. Those interactions serve to define local base pairing and also the overall pitch of the helix. Although, in solution, the average pitch of the helix is near to 10 base pairs, structural studies have revealed a high degree of variability and flexibility of pitch angle, including the modeling-based prediction that a flat, non-helical ribbon-like structure might form under conditions of extreme mechanical distension (Leger J F et al., 1999, Phys. Rev. Lett. 83:1066-1069; Bensimon D et al., 1995, Phys. Rev. Lett. 74:4754-4757; Smith SB et al., 1996, Science 271:795-799; Lebrun A et al., 1996, Nucl. Acids Res. 24:2260-2267; and Marko J F, Feig M, and Pettitt B M J. Phys. Chem., submitted (personal communication)) or upon the disruptive binding of an intercalator (Gao O et al., 1991, Proc. Natl. Acad. Sci. USA 88:2422-2426).

Summary of Invention Paragraph:
[0021] In some embodiments of the invention the device surface is a microarray. In some embodiments of the invention the device surface is a microbead. In some embodiments of the invention the device surface is an electrode. In some embodiments of the invention the device surface is an integrated circuit.

Detail Description Paragraph:
[0050] Although unexpected in a simple, mixed phase hybridization experiment as presented here, it is interesting to note that unwound ribbon-like duplexes have been proposed to exist transiently in other somewhat more extreme contexts. For instance, the DNA complex formed upon binding of intercalators such as ditercalinium, as revealed by X-ray crystallography (Gao O et al., 1991, Proc. Natl. Acad. Sci. USA 88:2422-2426), involves a nearly complete loss of helical winding. Similarly, an unwound and significantly extended double helix has been proposed to form in solution as a response to the mechanical stress induced by stretching (Leger J F et al., 1999, Phys. Rev. Lett. 83:1066-1069; Bensimon D et al., 1995, Phys. Rev. Lett. 74:4754-4757; Smith S B et al., 1996, Science 271:795-799; Lebrun A et al., 1996, Nucl. Acids Res. 24:2260-2267).

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L1: Entry 2 of 2 File: USPT Oct 7, 2003

US-PAT-NO: 6630306
DOCUMENT-IDENTIFIER: US 6630306 B1

TITLE: Bioreactive allosteric polynucleotides

DATE-ISSUED: October 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Breaker; Ronald R.	Guilford	CT		

US-CL-CURRENT: 435/6; 435/196, 435/287.2, 436/501, 536/23.1

CLAIMS:

What is claimed is:

1. A DNA polynucleotide comprising an allosteric site and an enzyme domain spatially distinct from said allosteric site, wherein reversible interaction of a chemical effecto with the allosteric site on the DNA polynucleotide reversibly alters the cleavage functi or configuration of the DNA polynucleotide, wherein the chemical effector is a metal ion or a small molecule having a molecular weight of 300 Daltons or less.

2. The DNA polynucleotide according to claim 1 wherein the function or configuration of the DNA polynucleotide is altered in less than 60 minutes after interaction with the chemical effector.

3. A DNA polynucleotide comprising an allosteric site and an enzyme domain spatially distinct from said allosteric site, wherein the rate of catalysis of the enzyme domain i reversibly modulated by interaction with a chemical effector, wherein the chemical effector is a metal ion or a small molecule having a molecular weight of 300 Daltons or less.

4. The DNA polynucleotide according to claim 3 wherein an observable change in the rate catalysis of the enzyme domain occurs in less than 6 minutes of interaction with the chemical effector.

5. The DNA polynucleotide according to claim 4 wherein the observable change occurs in less than 1 minute.

6. The DNA polynucleotide according to claim 1 or 3 wherein the chemical effector is selected from the group consisting of amino acids, amino acid derivatives, peptides, nucleosides, nucleotides, and steroids.

7. A biosensor comprising the DNA polynucleotide according to claim 1 or 3.

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8. A method for detecting the presence or absence of a compound or its concentration in sample comprising contacting the sample with a DNA polynucleotide comprising an alloster site and an enzyme domain spatially distinct from said allosteric site, wherein reversib interaction of the compound with the allosteric site alters the cleavage function or configuration of the polynucleotide relative to that of a control sample, and observing said alteration in the function or configuration of the DNA polynucleotide, wherein the chemical effector is a metal ion or small molecule having a molecular weight of 300 Daltons or less, and further wherein an alteration in function or configuration of the D polynucleotide indicates the presence or absence of a compound or its concentration in t sample.

9. The method according to claim 8 wherein the presence or absence of a compound or its concentration is detected by observation of an alteration in the cleavage function of th polynucleotide.

10. The method according to claim 8 wherein the chemical effector is selected from the group consisting of amino acids, amino acid derivatives, peptides, nucleosides, nucleotides, and steroids.

11. The DNA polynucleotide according to claim 3 wherein the rate of catalysis of the enzyme is measured by observing enzyme self-cleavage or substrate cleavage.

12. The biosensor according to claim 7, wherein the DNA polynucleotide is attached to a solid support.

13. An RNA polynucleotide comprising an allosteric site and an enzyme domain spatially distinct from said allosteric site, having three stem components, stem I, stem II and st III, wherein stem I and stem III are polynucleotide sequences which together form the enzyme domain and stem II is a polynucleotide sequence which forms the allosteric site, wherein interaction of a chemical effector with the allosteric site reversibly alters th cleavage function or configuration of the polynucleotide, further wherein the chemical effector is a metal ion or a small molecule having a molecular weight of 300 Daltons or less.

14. The polynucleotide according to claim 13 wherein the cleavage function or configuration of the polynucleotide is altered in less than 60 minutes after interaction with the chemical effector.

15. An RNA polynucleotide comprising an allosteric site and an enzyme domain spatially distinct from said allosteric site, having three stem components, stem I, stem II and st III, wherein stem I and stem III are polynucleotide sequences which together form the enzyme domain and stem II is a polynucleotide sequence which forms the allosteric site, wherein interaction of a chemical effector with the allosteric site reversibly modulates the rate of catalysis of the polynucleotide, further wherein the chemical effector is a metal ion or a small molecule having a molecular weight of 300 Daltons or less.

16. The polynucleotide according to claim 15 wherein an observable change in the rate of catalysis of the polynucleotide occurs in less than 6 minutes of interaction with the chemical effector.

17. The polynucleotide according to claim 16 wherein the observable change occurs in les than 1 minute.

18. The polynucleotide according to claim 15 wherein the chemical effector is selected from the group consisting of amino acids, amino acid derivatives, peptides, nucleosides, nucleotides, and steroids.

19. A biosensor comprising the polynucleotide according to claim 13 or 15.

20. A method for detecting the presence or absence of a compound or its concentration in sample comprising contacting the sample with a polynucleotide according to claim 13 or 1 such that reversible interaction of the compound with the allosteric site alters the cleavage function or configuration of the polynucleotide relative to that of a control sample, and observing said alteration in the cleavage function or configuration of the polynucleotide, wherein the compound is a chemical effector that is a metal ion or small molecule having a molecular weight of 300 Daltons or less and further wherein an alteration in function or configuration of the polynucleotide indicates the presence or absence of a compound or its concentration in the sample.

21. The method according to claim 20 wherein the presence or absence of a compound or it concentration is detected by observation of an alteration in the cleavage function of th polynucleotide.

22. The method according to claim 20 wherein the compound is a chemical effector that is selected from the group consisting of amino acids, amino acid derivatives, peptides, nucleosides, nucleotides, and steroids.

23. A polynucleotide according to claim 15 wherein the rate of catalysis of the enzyme i measured by observing enzyme self-cleavage or substrate cleavage.

24. A biosensor according to claim 19, wherein the polynucleotide is attached to a solid support.

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☐ 1. Document ID: US 20020187312 A1

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L4: Entry 1 of 5 File: PGPB Dec 12, 2002

PGPUB-DOCUMENT-NUMBER: 20020187312
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020187312 A1

TITLE: Matrix-free desorption ionization mass spectrometry using tailored morphology layer devices

PUBLICATION-DATE: December 12, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Fonash, Stephen J.	State College	PA	US	
Kalkan, Ali Kaan	State College	PA	US	
Cuiffi, Joseph	State College	PA	US	
Hayes, Daniel J.	State College	PA	US	

US-CL-CURRENT: 428/195.1; 428/220, 428/426, 428/446, 428/457, 428/689

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 20020058273 A1

L4: Entry 2 of 5 File: PGPB May 16, 2002

PGPUB-DOCUMENT-NUMBER: 20020058273
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020058273 A1

TITLE: Method and system for rapid biomolecular recognition of amino acids and protein sequencing

PUBLICATION-DATE: May 16, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Shipwash, Edward	San Francisco	CA	US	

US-CL-CURRENT: 435/6; 435/24, 435/287.1, 435/287.2

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Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 6689265 B2

L4: Entry 3 of 5 File: USPT Feb 10, 2004

US-PAT-NO: 6689265
DOCUMENT-IDENTIFIER: US 6689265 B2

TITLE: Electrochemical analyte sensors using thermostable soybean peroxidase

DATE-ISSUED: February 10, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Heller; Adam	Austin	TX		
Kenausis; Gregg L.	Austin	TX		
Chen; Qiang	Austin	TX		
Vreeke; Mark S.	Alameda	CA		

US-CL-CURRENT: 204/403.09; 204/403.04, 204/403.14

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 4. Document ID: US 6230792 B1

L4: Entry 4 of 5 File: USPT May 15, 2001

US-PAT-NO: 6230792
DOCUMENT-IDENTIFIER: US 6230792 B1

TITLE: Device for attaching an accessory to a heat exchanger

DATE-ISSUED: May 15, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Potier; Michel	Rambouillet			FR

US-CL-CURRENT: 165/121; 123/41.49, 165/135, 165/67, 180/68.4, 416/195

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 5. Document ID: US 3149370 A

L4: Entry 5 of 5 File: USOC Sep 22, 1964

US-PAT-NO: 3149370
DOCUMENT-IDENTIFIER: US 3149370 A

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TITLE: Animal slaughtering

DATE-ISSUED: September 22, 1964

INVENTOR-NAME: SAUVAGE JOHN E; ELLIOTT BRYAN S

US-CL-CURRENT: 452/54, 452/58, 452/65, 452/67

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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L15: Entry 1 of 1 File: USPT Aug 10, 1982

US-PAT-NO: 4343782
DOCUMENT-IDENTIFIER: US 4343782 A

TITLE: Cytological assay procedure

DATE-ISSUED: August 10, 1982

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shapiro; Howard M.	West Newton	MA	02165	

US-CL-CURRENT: 435/7.2; 250/302, 250/304, 356/39, 435/29, 436/63

CLAIMS:

What is claimed is:

1. A bioassay method for one or more non-excitable cells, said method comprising the steps of:

A. determining a characteristic of individual ones of said non-excitable cells representative of the membrane potential thereof by a non-intrusive method, and

B. comparing said cell characteristic to a reference characteristic to detect differences in the membrane potential of said individual cells,

wherein step A comprises the sub-steps of:

(i) incubating said cells with a cell membrane-permeant ionic dye, and

(ii) detecting an optical property of said individual cells, said optical property being representative of the intracellular dye level in the respective ones of said cells, and determining said cell characteristic from said optical property, and

wherein step B comprises the step of:

comparing said determined cell characteristic with said reference characteristic for said cells, and identifying differences in said determined cell characteristic with respect to said reference characteristic, said differences being representative of corresponding differences in cell membrane potential.

2. The method according to claim 1 wherein said detecting substep includes the step of detecting the intracellular concentration of said dye.

3. The method according to claim 2 comprising the further step of modifying said cells prior to sub-step (ii), whereby a change in cell membrane potential occurs prior to sub-step (ii).

4. The method according to claim 3 wherein said cell modification is physical.

5. The method according to claim 3 wherein said cell modification is pharmacological or chemical.

6. The method according to claim 3 wherein said cell modification is biological.

7. The method according to claim 3 wherein said modifying step precedes sub-step (i).

8. The method according to claim 3 wherein said modifying step succeeds sub-step (i).

9. The method according to claim 2 wherein said detecting sub-step (ii) comprises the sub-steps of:

detecting the amount of said dye within said one cell,

determining the volume of said one cell, and

determining from said detected amount and said determined volume the concentration of said dye within said one cell.

10. The method according to claim 2 wherein said detecting substep (ii) comprises the sub-steps of:

generating a first signal representative of the amount of said dye within said one cell,

generating a second signal representative of the volume of one of said cells,

generating a third signal representative of the ratio of said first and second signals, said third signal being representative of the concentration of said dye in said one cell.

11. The method according to claim 3 wherein said modification step comprises incubating said cells in a solution of ligands under conditions in which complementary cell receptors and said ligands bind.

12. The method according to claim 11 wherein said ligands include ligands selected from the group consisting of antigens, antibodies, haptens, allergens, and components of complement and said cells include cells of the immune system.

13. The method according to claim 11 wherein said ligands include one or more of the group of hormones, and natural or synthetic agonists or antagonists thereof.

14. The method according to claim 11 wherein said ligands include one or more

of the group consisting of pharmacological agents, and natural or synthetic agonists or antogonists thereof.

15. The method according to claims 9 or 10 wherein said dye is a fluorescent dye and wherein said dye detecting step includes the step of:

detecting fluorescence for one or more individual ones of said cells.

16. The method according to claims 9 or 10 wherein said dye is a fluorescent dye, and wherein said dye detecting step includes the step of:

detecting the spectral shift of fluorescence for one or more individual ones of said cells.

17. The method according to claims 9 or 10 wherein said dye detecting step includes the step of:

detecting optical absorption for one or more individual ones of said cells.

18. The method according to claims 9 or 10 wherein said dye detecting step includes the step of:

detecting the spectral shift of optical absorption of one or more individual ones of said cells following aggregation of said dye.

19. A bioassay method for one or more non-excitable cells, said method comprising the steps of:

A. determining a characteristic of individual ones of said non-excitable cells representative of the membrane potential thereof by a non-intrusive method, and

B. comparing said cell characteristic to a reference characteristic to detect differences in the membrane potential of said individual cells,

wherein step A includes the sub-steps of:

(a) incubating the cells with a dye which associates with individual cells, and

(b) detecting an optical characteristic of dye associated with the respective ones of said individual cells, said detected optical characteristics being indicative of the cell membrane potential of the respective ones of said individual cells.

20. The method of claim 1 or 2 or 19 wherein the reference characteristic comprises the results of an assay run in parallel with said cells.

21. The method of claim 19 wherein the reference characteristic is a value representative of a predetermined membrane potential and said comparison step determines the difference in magnitude between the detected potential and the potential corresponding to said reference characteristic.

22. The method of claim 19 wherein the reference characteristic is a value representative of a predetermined membrane potential and said comparison step

determines the direction of change between the detected membrane potential and the potential corresponding to said reference characteristic.

23. The method of claim 19 comprising the step of incubating said cells with a substance which induces a change in the membrane potential thereof, wherein the reference characteristic comprises a plurality of measurements representative of a predetermined time course of membrane potential change in a reference cell, a plurality of optical characteristic determinations are made on said cells, and said comparison step determines the difference in the time course of a potential change between said cells and said reference cell.

24. The method of claim 19 comprising the additional step of incubating said cells in a solution of ligands under conditions in which complementary cell receptors and ligand bind, said ligands being selected from the group consisting of neurotransmitters, hormones, agonists and antagonists thereof, immune system proteins, and combinations thereof.

25. A bioassay method for one or more non-excitable cells, said method comprising the steps of:

A. determining a characteristic of individual ones of said non-excitable cells representative of the membrane potential thereof by a non-intrusive method, and

B. comparing said cell characteristic to a reference characteristic to detect differences in the membrane potential of said individual cells,

wherein step A comprises the sub-steps of:

(i) incubating said cells with two or more cell membrane-permeant ionic dyes, and

(ii) detecting an optical property of said individual cells, said optical property being representative of the ratio of the intracellular levels of said dyes in the respective ones of said cells, and determining said cell characteristic from said optical property, and

wherein step B comprises the step of:

comparing said determined cell characteristic with said reference characteristic for said cells, and identifying differences in said determined cell characteristics with respect to said reference characteristic, said differences being representative of corresponding differences in cell membrane potential.

26. The method according to claim 25 wherein said detecting sub-step includes the step of detecting the intracellular concentrations of said dyes.

27. The method according to claim 26 comprising the further step of modifying said cells prior to sub-step (ii), whereby a change in cell membrane potential occurs prior to sub-step (ii).

28. The method according to claims 2 or 3 or 7 or 8 wherein said reference characteristic is a value representative of a predetermined concentration and said comparison step determines the difference in magnitude of said detected concentration and said predetermined concentration.

29. The method according to claims 2 or 3 or 7 or 8 wherein said reference characteristic is a value representative of a predetermined concentration and said comparison step determines the direction of change of the difference in magnitude of said detected concentration and said predetermined concentration.

30. The method according to claims 2 or 3 or 7 or 8 wherein said reference characteristic is a set of values representative of a predetermined concentration time course and said comparison step determines the differences in magnitude of said detected concentration and said predetemined concentration time course.

31. The method according to claim 28 including the further step of determining said reference characteristic by the steps of:

performing steps A and B for one or more control cells and determining said predetermined value, said predetermined value being representative of the concentration of said dye in said control cells.

32. The method according to claim 29 including the further step of determining said reference characteristic by the steps of:

performing steps A and B for one or more control cells and determining said predetermined value, said predetermined value being representative of the concentration of said dye in said control cells.

33. The method according to claim 30 including the further step of determining said reference characteristic by the steps of:

performing steps A and B for one or more control cells and determining said set of values, said set of values being representative of the time course of concentration of said dye in said control cells.

34. The method of claim 1 or 2 or 26 wherein said dye is a fluorescent dye and wherein said optical property detected is fluorescence.

35. The method of claim 34 wherein said dye is selected from the group consisting of cationic fluorescent dyes characterized by increasing fluorescence quantum efficiency in solvents of decreasing polarity.

36. The method of claim 34 wherein the concentration of dye in the extracellular solution is such as to minimize intracellular fluorescence quenching by the formation of complexes of reduced fluorescence.

37. The method of claim 1 or 2 or 26 wherein the dye is selected from the group consisting of fluorescent, cationic cyanine dyes.

38. The method of claim 37 wherein the dye is a salt of 3,3'dihexyl-2,2' oxacarbocyanine.

39. The method of claim 1 or 2 or 26 wherein the optical property measured is absorption.

40. The method of claim 1 or 2 or 19, said method being directed to the detection of the presence of a ligand in a solution, said method comprising the additional step of: incubating one or more non-excitable cells known to

contain a membrane bound receptor complementary to the ligand with said solution under conditions in which ligands and receptors bind, the presence of said ligand in said solution being indicated by a change in the membrane potential in the cells containing said receptor.

41. The method of claim 40 wherein the detected change in membrane potential is compared with a reference characteristic obtained by parallel assay of a solution containing a known concentration of said ligand to obtain a measure of the concentration of ligand in said solution.

42. The method of claim 1 or 2 or 19, said method being directed to the detection of the presence of cells having receptors complementary to a selected specific ligand in a plurality of cells heterogeneous with respect to ligand specificity, said method comprising the additional step of:

incubating said plurality of cells with a solution containing said specific ligand under conditions in which complementary cell receptors and ligands bind, the presence of said cells having receptors complementary to said ligand being indicated by a change in the membrane potential of said cells.

43. The method of claim 42 comprising the further step of segregating cells exhibiting similar membrane potential changes to produce a cell population rich in cells sensitive to said selected ligand.

44. The method of claim 1 or 2 or 19, said method being directed to the detection of the presence in a cell population of cells having receptor sites complementary to a selected ligand but a different physiological response thereto, said method comprising the additional step of:

incubating said cell population with a solution containing said selected ligand to induce membrane potential changes in said cells of distinct magnitudes or directions.

45. The method of claim 44 comprising the further step of segregating cells exhibiting similar membrane potential changes to produce a cell population rich in cells sensitive to said selected ligand.

46. The method of claim 1 or 2 or 19, said method being directed to the comparison of the physiological response of a cell population exposed to plural chemically distinct ligands, said method comprising the additional steps of:

incubating samples of said cell population with respective ligands under conditions in which receptors and ligands bind; and monitoring changes in membrane potential in individual cells of respective cell samples.

47. The method of claim 1 or 2 or 19, said method being directed to the determination of the cumulative effect of exposing plural chemically distinct ligands to a population of cells, said process comprising the additional step of;

incubating the ligands and the cell population under conditions in which complementary cell receptors and ligands bind.

48. The method of claim 1 or 2 or 19, said method being directed to the determination of the viability of a cell population after exposure to a cell toxin, said method comprising the further step of:

incubating the cell population with said toxin.

49. The method of claim 46 wherein plural determinations of the membrane potential of cells in said population are made at intervals after exposure to said toxin.

50. The method of claim 1 or 2 or 19, said method being directed to the determination of the effect on a cell population after exposure to a cell nutrient, said method comprising the further step of:

incubating the cell population with said nutrient.

51. The method of claim 48 wherein plural determinations of the membrane potential of cells in said population are made at intervals after exposure to said nutrient.

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First Hit

L8: Entry 2 of 19 File: PGPB Apr 1, 2004

PGPUB-DOCUMENT-NUMBER: 20040063220
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040063220 A1

TITLE: Substrate chemistry for protein immobilization on a rigid support

PUBLICATION-DATE: April 1, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lebrun, Stewart J.	Irvine	CA	US	

US-CL-CURRENT: 436/518; 435/287.2

CLAIMS:

What is claimed is:

1. A substrate for protein immobilization, comprising a rigid support and a hydrophobic polymeric layer attached to said rigid support, wherein said hydrophobic polymeric layer has a surface chemistry adapted to immobilize a protein sample and wherein said substrate is configured to allow immobilization of a plurality of protein samples on discrete addressable spots thereon.

2. The substrate of claim 1, wherein said hydrophobic polymeric layer is a PVDF layer.

3. The substrate of claim 2, wherein the thickness of the PVDF layer is about 100-250 .mu.m.

4. The substrate of claim 2, wherein the PVDF layer has a pore size of 0.2 to 0.45 .mu.m.

5. The substrate of claim 2, wherein the PVDF layer is a sheet, a membrane, or is formed from PVDF pellets.

6. The substrate of claim 1, wherein said hydrophobic polymeric layer produces a background signal upon protein imaging using visual or fluorescent light of less than about 100 lumens.

7. The substrate of claim 1, wherein said hydrophobic polymeric layer produces a background signal upon protein imaging using visual or fluorescent light of between about 0 and 50 lumens.

8. The substrate of claim 1, wherein said hydrophobic polymeric layer produces a background signal upon protein imaging using visual or fluorescent light of between about 0 and 15 lumens.

9. The substrate of claim 1, wherein the rigid support is a silanated material.

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10. The substrate of claim 1, wherein the rigid support is glass or plastic.

11. The substrate of claim 1, further comprising a bar code.

12. The substrate of claim 1, further comprising a removable protective film for protecting the hydrophobic polymeric layer and any protein samples immobilized thereon.

13. The substrate of claim 1 which further comprises a template attached to the rigid support, wherein said template divides said hydrophobic polymeric layer into at least two distinct sections, each section being configured to allow immobilization of a plurality of protein samples, and wherein said template is adapted to allow application of different chemical reagents to the at least two distinct sections of the polymeric layer.

14. A method of preparing a protein array, comprising the step of spotting a plurality of protein samples at discrete, addressable locations onto the PVDF layer of the substrate of claim 2, wherein the PVDF layer is in a dry state.

15. A method of making a PVDF-coated rigid substrate adapted to immobilize a plurality of bioactive molecules, comprising: applying an adhesive layer to a rigid support; adhering a PVDF membrane sheet to said adhesive layer on said rigid support; drying; and cutting excess PVDF membrane sheet away from the rigid support, to form the PVDF-coated rigid substrate.

16. The method of claim 15, wherein the adhesive is selected from the group consisting of a double-sided inert adhesive microfilm, a silicone, a glue, a double-sided tape and direct chemical bonding.

17. The method of claim 15, wherein the rigid support is glass or plastic.

18. The method of claim 15, further comprising attaching a template to the PVDF-coated rigid substrate.

19. The method of claim 18, wherein the template provides from about 2-500 wells.

20. An array-based kit for screening a patient for a plurality of autoimmune diseases, said kit comprising a substrate having a layer of PVDF attached to a rigid support, said layer of PVDF having a plurality of protein antigens related to said autoimmune diseases immobilized thereon at different known locations; and a reagent for detecting the binding of an antibody from the patient to the protein antigens.

First Hit

L8: Entry 1 of 19 File: PGPB Apr 15, 2004

PGPUB-DOCUMENT-NUMBER: 20040072274
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040072274 A1

TITLE: System and method for visualization and digital analysis of protein and other macromolecule microarrays

PUBLICATION-DATE: April 15, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lebrun, Stewart J.	Irvine	CA	US	

US-CL-CURRENT: 435/21

CLAIMS:

What is claimed is:

1. A method for visualization and digital analysis of sample interactions with a biological array, comprising: allowing the sample to interact with the array, which comprises biological molecules immobilized on a solid substrate in a two-dimensional and addressable pattern; contacting the array with a secondary detector molecule comprising an enzyme; incubating the array with a developing agent comprising a substrate of the enzyme, such that the enzyme catalyzes a reaction wherein the substrate is converted to a detectable product; digitizing an array image created by the detectable product by scanning the array on a digital scanner; and analyzing the digital image.

2. The method of claim 1, wherein the detectable product is selected from the group consisting of a colorometric precipitate, a colorometric enzyme-analyte, a colorometric dye-analyte, a colorometric intermediate-analyte, and a radioactive-analyte.

3. The method of claim 1, wherein prior to contacting the array with the secondary detector molecule, the array is washed to remove unreacted sample.

4. The method of claim 1, wherein prior to digitizing the array image, the array is washed to terminate the reaction.

5. The method of claim 1, wherein prior to digitizing the array image, the array is dried.

6. The method of claim 1, wherein the enzyme is Alkaline Phosphatase.

7. The method of claim 1, wherein the substrate is BCIP/NBT.

8. The method of claim 1, wherein the scanner is selected from the group consisting of Epson PERFECTION 1650, Canon CANOSCAN N1240U, and Hewlett-Packard SCANJET 5300C.

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9. The method of claim 1, wherein prior to scanning the array, the array is placed together with one or more additional arrays in a template having from about 1 to 20 array slots.

10. The method of claim 1, wherein the array is labeled with a barcode.

11. The method of claim 1, further comprising correcting for user error and slide variations using an imaging program.

12. The method of claim 1, further comprising quantifying markers to construct a standard curve, such that visual intensity can be converted into molecular mass.

13. The method of claim 12, wherein a clinical index is calculated by dividing the molecular mass by the dilution factor.

14. A method for analysis of sample interactions with a protein microarray, comprising: allowing the sample to interact with the microarray, comprising a plurality of proteins immobilized on a solid substrate in a two-dimensional and addressable pattern, the solid substrate comprising a barcode for sample identification and a PVDF membrane adhered to a rigid support; contacting the microarray with a secondary detector molecule comprising a selective binding moiety and an enzyme conjugated thereto; washing the microarray to remove unbound secondary detector molecules; incubating the array with a developing agent comprising a substrate of the enzyme, such that the enzyme catalyzes a reaction wherein the substrate is converted to a detectable product; washing the microarray to terminate the reaction and remove unreacted developing agent; scanning the microarray using a digital scanner to create a digital image of the microarray; and analyzing the digital image which corresponds to the sample interactions with the protein microarray.

15. A system for analysis of autoimmune diseases in humans, comprising: a microarray, comprising a plurality of autoimmune markers immobilized on a solid substrate in a two-dimensional and addressable pattern, the solid substrate comprising a PVDF membrane adhered to a rigid support; a first reagent comprising anti-human IgG conjugated to an enzyme; a second reagent comprising a developing agent comprising a substrate of the enzyme, wherein the first and second reagents react when combined to yield a colorometric change; and a flatbed digital scanner.

16. A system for analysis of sample interactions with a biological array, comprising: an array, comprising a plurality of biological molecules immobilized on substrate in a two-dimensional and addressable pattern, the substrate comprising a rigid support which has an opaque surface or has been modified to have an opaque surface, said surface being adapted to bind the plurality of biological molecules; a flatbed scanner adapted to produce a digital image of the array; and a software program adapted to quantify and analyze the digital image.

L16: Entry 6 of 10 File: USPT Aug 25, 1998

US-PAT-NO: 5798030
DOCUMENT-IDENTIFIER: US 5798030 A

TITLE: Biosensor membranes

DATE-ISSUED: August 25, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Raguse; Burkhard	Gordon			AU
Cornell; Bruce A	Neutral Bay			AU
Braach-Maksvytis; Vijoleta L	Dulwich Hill			AU
Pace; Ronald J	Farrer			AU

US-CL-CURRENT: 204/403.08; 204/403.1, 204/415, 204/418, 435/287.1, 435/289.1, 435/817

CLAIMS:

We claim:

1. A biosensor for use in detecting the presence or absence of an analyte in a sample, t biosensor comprising an electrode and a bilayer membrane comprising a top layer and a bottom layer, the bottom layer being proximal to and connected to the electrode such tha a space exists between the membrane and the electrode, the conductance of the membrane being dependent on the presence or absence of the analyte, the membrane comprising a closely packed array of amphiphilic molecules and a plurality of ionophores dispersed therein, and a layer of a hydrogel formed on top of the lipid bilayer membrane, the hydrogel allowing the passage of the analyte molecule to be detected.

2. A biosensor as claimed in claim 1 in which the hydrogel is a thermosetting gel.

3. A biosensor as claimed in claim 2 in which the thermosetting gel is an agar gel.

4. A biosensor as claimed in claim 2 in which the gel contains between 0.3-5% agar.

5. A biosensor as claimed in claim 2 in which the thermosetting gel is a gelatine gel.

6. A biosensor as claimed in claim 1 in which the hydrogel is an in situ polymerised hydrogel.

7. A biosensor as claimed in claim 1 in which the hydrogel is an acrylic acid or an acrylic acid derivative that is polymerised by free radial polymerisation.

8. A biosensor as claimed in claim 1 in which the hydrogel is formed from acrylamide and bisacrylamide cross-linker.

9. A biosensor as claimed in claim 1 in which the hydrogel is formed from cross-linked hydroxyethyl acrylate or hydroxyethyl methacrylate or other biocompatible gel.

10. A biosensor as claimed in claim 1 in which the ionophore is capable of transporting ion that is produced by the reaction of an enzyme with its substrate, said enzyme being either covalently or non-covalently attached to the hydrogel.

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L9: Entry 6 of 44 File: USPT Apr 15, 1997

US-PAT-NO: 5620856
DOCUMENT-IDENTIFIER: US 5620856 A
**** See image for Certificate of Correction ****

TITLE: Monoclonal antibody assay and kit for detecting metal cations in body fluids

DATE-ISSUED: April 15, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Carlson; Randall R.	Lincoln	NE		
Stout; Jay S.	Lincoln	NE		
Wylie; Dwane E.	Lincoln	NE		
Wagner; Fred W.	Walton	NE		
Riddell; Malcolm	Vero Beach	FL		

US-CL-CURRENT: 435/7.1; 435/337, 435/338, 435/343, 435/7.4, 435/7.9, 435/7.92, 530/388.1, 530/388.26

CLAIMS:

What is claimed is:

1. A method for detecting a metallic cation in a sample of a body fluid of an animal, which comprises:

contacting an effective amount of a first antibody specific for an endogenous naturally occurring polypeptide with the sample of body fluid containing the metallic cation to fo a first antigen-antibody complex, wherein the endogenous naturally occurring polypeptide is capable of binding the metallic cation;

adding an effective amount of a second antibody specific for an epitope on a cation/polypeptide complex to the first antigen-antibody complex to form a second antige antibody complex, wherein the cation/polypeptide complex is formed from the metallic cation and the endogenous naturally occurring polypeptide, and the second antibody does not substantially cross-react with an epitope found on the endogenous naturally occurrin polypeptide alone; and

detecting the metallic cation in the body fluid by determining the amount of the second antigen-antibody complex.

2. The method of claim 1 wherein the metallic cation is a transition metal, a Group IIIa metal/metalloid, or a Group IVa metal/metalloid.

3. The method of claim 2 wherein the metallic cation is a lead cation.

4. The method of claim 1 wherein the first antibody is a polyclonal antiserum specific f blood proteins.

5. The method of claim 1 further comprising:

lysing cells in the sample of the body fluid with a lysing agent to provide for release the endogenous naturally occurring polypeptide that binds the metallic cation.

6. The method of claim 1 wherein the body fluid includes blood, urine, saliva or cerebrospinal fluid.

7. The method of claim 1 wherein the first antibody is an antibody specific for .delta.-aminolevulinic acid dehydratase (ALAD).

8. The method of claim 1 wherein the second antibody is a monoclonal antibody specific f a lead cation/.delta.-aminolevulinic acid dehydratase complex.

9. The method of claim 1 wherein the first antibody is immobilized on a substrate.

10. The method of claim 1 wherein the second antibody has a dissociation constant of abo 10.sup.-4 to about 10.sup.-13.

11. The method of claim 1 wherein detecting the metallic cation in the body fluid comprises determining the amount of the metallic cation.

12. The method of claim 1 wherein the second antibody is labelled with a detectable agen

13. The method of claim 1 wherein the second antibody is specific for an epitope found o an endogenous naturally occurring polypeptide portion of the cation/polypeptide complex is specific for a combination of the metallic cation and a polypeptide portion coordinat with the metallic cation within the cation/polypeptide complex.

14. The method of claim 1 wherein the second antibody is specific for a metallic cation portion of the cation/polypeptide complex.

15. The method of claim 1 further comprising:

incubating the second antigen-antibody complex with a third antibody specific for an immunoglobulin to form a third antigen-antibody complex, said third antibody being label with a detectable agent; and

wherein detecting the metallic cation comprises determining the amount of the third antigen-antibody complex by detecting the detectable agent.

16. The method of claim 1 wherein the first antibody is an antibody specific for hemoglobin, human serum albumin, transferrin, glutathione, or protein kinase C.

17. A method for detecting a metallic cation in a sample of a body fluid of an animal, which comprises:

contacting an effective amount of a first antibody specific for a first epitope on a cation/polypeptide complex with the sample of body fluid containing the metallic cation form a first antigen-antibody complex, said cation/polypeptide complex being formed from the metallic cation and an endogenous naturally occurring polypeptide;

adding an effective amount of a second antibody to the first antigen-antibody complex to form a second antigen-antibody complex, wherein the second antibody is specific for a second epitope on the cation/polypeptide complex; and

detecting the metallic cation in the sample of body fluid by determining the amount of t second antigen-antibody complex.

18. A method for detecting a metallic cation in a sample of a body fluid of an animal, which comprises:

contacting an effective amount of a first antibody with the sample of body fluid containing the metallic cation to form a first antigen-antibody complex, said first antibody being specific for an epitope of a cation/polypeptide complex, wherein the cation/polypeptide complex is formed from the metallic cation and an endogenous naturall occurring polypeptide, and the epitope is not found on an uncomplexed form of the endogenous naturally occurring polypeptide;

adding an effective amount of a second antibody to the first antigen-antibody complex to form a second antigen-antibody complex, wherein the second antibody is specific for the endogenous naturally occurring polypeptide; and

detecting the metallic cation in the sample of the body fluid by determining the amount the second antigen-antibody complex.

19. A method for detecting a metallic cation in a sample of body fluid of an animal, whi comprises:

contacting an effective amount of a capture antibody with the sample of body fluid containing the metallic cation to form a first antigen-antibody complex, wherein the fir antibody is specific for an epitope on an endogenous naturally occurring enzyme capable binding the metallic cation, and the metallic cation inhibits activity of the enzyme;

restoring the enzyme activity in the antigen-antibody complex by removing the metallic cation; and

detecting the metallic cation in the sample of body fluid by assaying the restored enzym activity.

20. A kit for detecting a metallic cation in a sample of a body fluid from an animal, which comprises:

an antibody specific for a naturally occurring enzyme, wherein the enzyme is capable of binding the metallic cation;

an agent capable of restoring the activity of the enzyme by removing the metallic cation from the enzyme; and

a substrate for the enzyme.

21. A kit according to claim 19, wherein the metallic cation is a lead cation, the naturally occurring enzyme is .delta.-aminolevulinic acid dehydratase, and the substrate is .delta.-aminolevulinic acid.

22. An antibody specific for an epitope on a metallic cation naturally occurring polypeptide complex, said antibody being produced by hybridoma call line ATCC No. HB

11330.

23. A hybridoma having ATCC No. HB11330.

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L44 ANSWER 1 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:182375 HCAPLUS
DOCUMENT NUMBER: 140:213595
TITLE: Molecular **bioswitch** for detecting protein interactions using **electrical** conductivity
INVENTOR(S): Lebrun, Stewart J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004043427	A1	20040304	US 2003-608903	20030627 <--
PRIORITY APPLN. INFO.:			US 2002-393195P P	20020701 <--

AB Preferred aspects of the present invention relate to a method for detection and quantification of mol. interactions between proteins **bound** to a support and ligand mols., in particular antibodies, in a test sample. More particularly, the preferred methods takes advantage of the **elec.** conductivity of **metal**-antibody conjugates.
IC ICM G01N033-53
NCL 435007100
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 14, 15
ST mol **bioswitch** detecting protein interaction **elec** cond
IT Antibodies and **Immunoglobulins**
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IgG; mol. **bioswitch** for detecting protein interactions using **elec.** conductivity)
IT Samples
(Test; mol. **bioswitch** for detecting protein interactions using **elec.** conductivity)
IT **Antigens**
RL: ARG (Analytical reagent use); DEV (Device component use); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process); USES (Uses)
(autoantigens; mol. **bioswitch** for detecting protein interactions using **elec.** conductivity)
IT Molecules
(**bioswitch**; mol. **bioswitch** for detecting protein interactions using **elec.** conductivity)
IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**conjugates**, with **metal**; mol. **bioswitch** for detecting protein interactions using **elec.** conductivity)
IT Autoimmune disease
Diagnosis
Disease, animal
Electric conductivity
Electric current
Electric potential
Electrodes
Immobilization, molecular or cellular
Mammalia

Molecules
Protein degradation
Reaction
(mol. **bioswitch** for detecting protein interactions using **elec.** conductivity)

IT **Antigens**
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(mol. **bioswitch** for detecting protein interactions using **elec.** conductivity)

IT Antibodies and **Immunoglobulins**
RL: ANT (Analyte); DGN (Diagnostic use); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(mol. **bioswitch** for detecting protein interactions using **elec.** conductivity)

IT Ligands
Proteins
RL: ANT (Analyte); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent)
(mol. **bioswitch** for detecting protein interactions using **elec.** conductivity)

IT **Metals**, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(mol. **bioswitch** for detecting protein interactions using **elec.** conductivity)

L44 ANSWER 2 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2004-14630 BIOTECHDS
TITLE: Electrically coupling an electrode pair in several electrode pairs in a biosensor with a macromolecule e.g. nucleic acid, protein or carbohydrate;
useful for detecting a **binding** event between e.g. nucleic acid and protein
AUTHOR: FREEMAN B A; PISHARODY S
PATENT ASSIGNEE: FREEMAN B A; PISHARODY S
PATENT INFO: US 2004048241 11 Mar 2004
APPLICATION INFO: US 2002-330445 26 Dec 2002
PRIORITY INFO: US 2002-330445 **26 Dec 2002**; US 2001-297583 11 Jun 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-313886 [29]
AN 2004-14630 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Electrically coupling an electrode pair (EP) in several EPs in biosensor with macromolecule (M) derivatized with first and second reactive groups (G1,G2) involves: (i) applying a first voltage at a first electrode in EP to unmask G1 which **binds** to first electrode thus linking (M) to first electrode, and (ii) applying second voltage at second electrode in EP to unmask G2.
DETAILED DESCRIPTION - Electrically (M1) coupling EP in several EPs in a biosensor with (M), (A) where EP comprises a first electrode and a second electrode, a first portion of (M) is derivatized with first reactive group (122) and a second portion of (M) is derivatized with second reactive group (125), and G1 is masked with a first electrolabile masking group (124) and G2 is masked with a second electrolabile masking group (126); and the method comprises (A) - (C): (A) (A): (i) applying a first voltage at the first electrode in EP under conditions that are sufficient to unmask G1, where the unmasked G1 **binds** to the first electrode thus linking (M) to the first electrode; and (ii)

applying a second voltage of the second electrode in EP under conditions that are sufficient to unmask G2, where the unmasked G2 **binds** to the second electrode thus electrically coupling EP in the biosensor with (M); or (B) (B) (where EP comprises a first electrode and a second electrode, an intercalator is covalently linked to the second electrode, and a portion of (M) is derivatized with a reactive group that is masked with an electrolabile masking group): (i) applying a voltage at the first electrode in EP under conditions that are sufficient to unmask the reactive group, where the unmasked reactive group **binds** to the first electrode thus linking (M) to the first electrode; and (ii) exposing EP to a solution that potentially comprises an analyte for a period of time, where, when the analyte **binds** to (M) to form a complex comprising (M) and the analyte, the intercalator **binds** to the complex thus electrically connecting EP; or (C) (C) (where EP comprises a first electrode and a second electrode, a first portion of (M) is derivatized with G1 and a second portion of (M) is derivatized with G2, and G1 is masked with an electrolabile masking group and G2 is masked with a photosensitive or chemically sensitive masking group): (i) applying a voltage at the first electrode in EP under conditions that are sufficient to unmask the reactive group, where the unmasked reactive group **binds** to the first electrode thus linking (M) to the first electrode; and (ii) exposing EP to a light source or a chemical thus unmasking G2, where the unmasked G2 **binds** to the second electrode thus electrically coupling EP in the biosensor with (M).

WIDER DISCLOSURE - (1) a kit for performing (M1); and (2) interfacing a biosensor with data acquisition and signal generation equipment.

BIOTECHNOLOGY - Preferred Method: In (M1), the first voltage and second voltage are different. The first electrode and second electrode are separated by a distance of about 10-10000Angstrom, preferably 30-500Angstrom, and more preferably 50-200Angstrom. The first and second electrode have a resistivity of less than 104 ohm meters. The first and second electrode are each made from the same or different material that are each independently chosen from silicon, dense silicon carbide, boron carbide, Fe3O4, germanium, silicon germanium, silicon carbide, polysilicon, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide, mercury cadmium telluride, tellurium, selenium, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe, CdTe, GaAs, InP, GaSb, InAs, Te, PbS, InSb, PbTe, PbSe, and tungsten disulfide. The first and second electrode are made of a **metal.** The first electrode and the second electrode are each made from the same or different material that are each independently chosen from ruthenium cobalt, rhodium, rubidium, lithium, sodium potassium, vanadium, cesium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and carbon nanotube and its alloy. The G1 and G2 are the same or different material and are each independently chosen from sulfate, sulfonate, sulfonyl moiety, thiol, thioether, sulfur-containing moiety, chalcogen-containing moiety, amine, carbonyl-containing moiety, carboxylic acid, aldehyde, ketone, phosphate, phosphonate, phosphorothioate, pnictogen moiety, silane, silicon-containing moiety, alkene, alkyne, hydroxy group and halogen. The G1 and G2 are each a thiol. The first electrolabile masking group and the second electrolabile masking group are different and are chosen from S-2,2,2-trichloroethoxycarbonyl derivative, S-benzyloxycarbonyl derivative, S-benzylthioether derivative, S-triphenylmethyl thioether derivative, S-2,4,6-trimethoxybenzyl thioether derivative, and S-2-picolyl N-oxide thioether derivative. (M1) further involves testing for background conductance between the first and second electrode, exposing EP to a

solution that potentially comprises an analyte for a period of time, drying EP, and measuring a current through EP. The period of time is less than 30 minutes, between one minute and one hour or between one hour and fifteen hours. The (M) is a single stranded nucleic acid and the analyte is a single stranded nucleic acid that has sufficient complementarity to (M) to **bind** to (M) in the exposing step. The (M) is a single stranded nucleic acid and the analyte is a single stranded nucleic acid that has sufficient complementarity to (M) to **bind** to (M) under conditions of high, intermediate or low stringency. The drying step further involves blowing nitrogen or argon gas on EP. The measuring step further involves quantifying a current across EP when a voltage of between +/- 5 volts is applied across EP. The analyte comprises a whole cell, subcellular particle, virus, prion, viroid, nucleic acid, protein, **antigen**, lipoprotein, lipopolysaccharide, lipid, glycoproteins, carbohydrate moiety, cellulose derivative, an **antibody**, fragment of an **antibody**, peptide, hormone, pharmacological agent, cellular component, an organic compound, a non-biological polymer, a synthetic organic molecule, an organo-**metallic** compound, or an inorganic molecule. The applying step are repeated with a different EP in several EPs using a different (M), where the different EP comprises a first electrode and a second electrode, a first portion of the different (M) is derivatized with a third reactive group and a second portion of (M) is derivatized with a fourth reactive group, and the third reactive group is masked with a third electrolabile masking group and the fourth reactive group is masked with a fourth electrolabile masking group. The intercalator comprises ethidium, ethidium derivative, ethidium complex, acridine, acridine derivative or an acridine complex. The intercalator comprises acridine orange, acridine yellow, 9-aminoacridine, hydrochloride hydrate, 2-aminoacridone, 9,9'-biacridyl, 9-chloroacridine, 6,9-dichloro-2-methoxyacridine, n-(1-leucyl)-2-aminoacridone, etc. (M1) further involves drying EP, and measuring a current through EP. The applying step is repeated before the exposing step with a different EP in several EPs using a different (M), where the different EP comprises a first electrode and a second electrode, a portion of the different (M) is derivatized with a reactive group that is masked with a electrolabile masking group. The applying step and exposing step are repeated with a different EP in several EPs using a different (M). The G2 is masked with a photosensitive masking group and the light source is ultraviolet or laser light. The G2 is masked with a photosensitive masking group having the formula (F1). A = -OH, substituted or unsubstituted alkoxy, -OC(O)CH3, -NH2, or -NHCH3; X1, X2 = H, Cl, Br, or I, at least one of X1 and X2 being Cl, Br or I; Q = -O-, -NH-, or -NCH3-; Y1 = -H, -Cl, -Br, -I, -C(O)OH, -NO2, -C(O)NHR1, -CN, -C(O)H, -C(O)CH3, benzoxazol-2-yl, benzothiazol-2-yl, or benzimidazol-2-yl; Y2 = -H, -C(O)OH, or -SO3H; M1 = -H, -CH3, -NR2R3, -C(O)NR2R3, or -COOH; Z = second reactive group; M2 = -H or Z and M2 together are =N2, =O, or =NNHR1; and R1, R2 and R3 = substituted or unsubstituted moiety chosen from 1-20C alkyl, 2-20C alkenyl, 2-20C alkynyl, 1-20C alkoxy, 1-20C alkoxy, 1-20C alkylsulfonyl, 4-16C arylsulfonyl, 2-20C heteroalkyl, 2-20C heteroalkenyl, 3-8C cycloalkyl, 3-8C cycloalkenyl, 4-16C aryl, 4-16C heteroaryl and 2-30C heterocyclyl. The G2 is masked with a chemically sensitive masking group and G2 and the chemically sensitive masking group together form a moiety chosen from S-alkyl thioether having the formula CnH(2n+1)SR, S-benzyl thioether having the RSCH2Ph, and S-diphenylmethyl thioether having the formula RSCH(C6H5)2, where R is the macromolecule and the exposing step cleaves the moiety thus unmasking G2. The applying step and the exposing step are repeated with a different EP in several EPs using a different (M), where the different EP comprises a first electrode and a second electrode, a first portion of the different (M) is derivatized with G1 and a second portion of (M) is derivatized with G2, and G1 is masked with

a electrolabile masking group and G2 is masked with a photosensitive or chemically sensitive masking group. The applying step is repeated with a different EP in several EP using a different (M) prior to the exposing step.

USE - (M1) Is useful for electrically coupling an electrode pair in several electrode pairs in a biosensor with a macromolecule such as a nucleic acid, a protein, polypeptide, peptide, an **antibody**, carbohydrate, polysaccharide, lipid, fatty acid or a sugar (claimed). (M1) Is useful for detecting macromolecule/analyte **binding** events such as nucleic acid/protein interactions. (51 pages)

L44 ANSWER 3 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2004-15971 BIOTECHDS
TITLE: Device useful for the preparation of sensor comprises a substrate containing a **metal** layer having at least two regions attached with different species, forming a mixed self-assembled monolayer on the **metal** layer; biosensor production useful for analysis
AUTHOR: FREDERIX F
PATENT ASSIGNEE: INTERUNIV MICRO-ELECTRONICA CENT VZW
PATENT INFO: EP 1413886 28 Apr 2004
APPLICATION INFO: EP 2002-447203 25 Oct 2002
PRIORITY INFO: EP 2002-447203 **25 Oct 2002**; EP 2002-447203 25 Oct 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
AN 2004-15971 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A device for the preparation of sensor comprising a substrate containing a **metal** layer having at least two regions attached with different species, forming a mixed self-assembled monolayer on the **metal** layer, is new.

DETAILED DESCRIPTION - A device for the preparation of sensor comprises a substrate containing a **metal** layer. The **metal** layer comprises at least two regions. A first species of formula X-R1-S-S-R2-Y (I) is attached to a first region. A second species of formula W-R3-S-S-R4-Z (II) is attached to a second region. The first and second species forms a mixed self-assembled monolayer on the **metal** layer. R1 and R2 = spacer of n carbon atoms (optionally interrupted by p heteroatoms); n and p = integer; X = -C(=O)-O-pyrrolidin-2,5-dion-1-yl; Y = an organic group; R3 and R4 = spacer optionally interrupted by a heteroatom; and W and Z = organic group. Provided that n or n+p is greater than 11. INDEPENDENT CLAIMS are also included for: (1) production (P1) of a device suitable for determining the presence of a target molecule involving subjecting a substrate containing at least a **metal** layer to a species of formula (I) to form a self-assembled monolayer on the substrate; and (2) compound of formula (I).

BIOTECHNOLOGY - Preferred Component: The recognition molecule is a chemical compound with a free NH2 group (preferably **antigen**, **antibody**, nucleic acid strand, hormone, enzyme or polyaminoacid). m' = integer (greater than 7, preferably 10).

USE - The device is useful for the preparation of a sensor (claimed).

ADVANTAGE - The device performs highly sensitive and selective analysis; and gives high reproducibility sensor.

EXAMPLE - 16,16'-Dithiohexadecanoic acid di(N-hydroxysuccinimide ester) (A) was deposited on a gold layer on a substrate, from a water-free organic solvent, tetrahydrofuran (THF). The **metal** substrates were deposited in this solution and the thiols were organized

on a self-assembled monolayer (SAM) in at least 3 hours. The substrate with the SAM was rinsed with THF and dried with nitrogen. The substrate was put in a solution with a recognition molecule, 16-(15-(2,5-dioxo-pyrrolidin-1-yloxycarbonyl)-pentadecyldisulfanyl)-hexadecanoic acid 2,5-dioxo-pyrrolidin-1-yl ester, which was covalently **bound** without any activation step. The contact angle of the molecule on the gold surface was 43+/-1 degrees. As comparative a self-assembling monolayer of 16-mercapto-hexadecanoic acid deposited on the substrate having a gold layer was converted to a self-assembling monolayer comprising a N-hydroxysuccinimidyl ester from carboxylic acid groups of the self-assembling layer. The ester was coupled to the free amine group of the protein. The **immobilization** of **antibodies** on (A)/comparative was greater than 4383+/-13 pg/mm2/130 - 200 ng/cm2. Thus **immobilization** degree was very high for **antibodies** on (A). (24 pages)

L44 ANSWER 4 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:414788 HCAPLUS
DOCUMENT NUMBER: 140:402821
TITLE: Methods, device and instrument for detection of analytes
INVENTOR(S): Feldmann, Jochen; Franzl, Thomas; Klar, Thomas; Raschke, Gunnar; Soennichsen, Carsten; Kowarik, Stefan; Nichtl, Alfons; Kuerzinger, Konrad
PATENT ASSIGNEE(S): Ludwig-Maximilian-Uni Versitaet Muenchen, Germany; Roche Diagnostics GmbH
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004042403	A2	20040521	WO 2003-EP12234	20031103 <--
WO 2004042403	A3	20040729		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-24379 A 20021104 <--
EP 2003-5005 A 20030305

AB The present invention relates to a method, a device and an instrument for the detection of an analyte (4) in a sample (6). Such method, device and instrument is used in clin. diagnostics, pharmacol., e.g. drug screening, environmental anal. as well as in other fields of anal. like chemical or biochem. According to the present invention, the method for detection of an analyte (4) in a sample comprises the following steps of (a) providing at least one particle structure (1) detectable by light scattering and coated with **binding** entities (2) for said analyte (4); (b) contacting the at least one particle structure (1) with the sample (6), (c) illuminating the at least one particle structure (1) and measuring the

scattered light emitted by individual particle structures (1) at least twice and (d) determining a change in the spectral signature of the scattered light as a measure of the presence and/or quantity of the analyte (4) in the sample (6). In order to detect more than one analyte (4) simultaneously, particle structures (1) of different classes of particle structures may be coated with different **binding** entities. Further, instead of coating the particle structure (1) with **binding** entities specific for the analyte (4), the particle structure (1) may be coated with substances (21) competing with said analyte (4) for **binding** to specific **binding** entities (2). Any competitive and non-competitive assay format can be put into practice. A biotin-streptavidin affinity **biosensor** was prepared and used light scattering spectroscopy of single gold nanoparticles.

IC ICM G01N033-58

CC 9-1 (Biochemical Methods)
Section cross-reference(s): 1, 79, 80

ST device instrument detection analyte; biotin streptavidin **biosensor** gold nanoparticle scattering spectroscopy

IT Samples
(anal. of; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Diodes
(array; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Antibodies and **Immunoglobulins**
Antigens
Peptides, analysis
Proteins
RL: ANT (Analyte); ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as **binding** agent and/or signal enhancing agent; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Nucleic acids
Peptide nucleic acids
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as **binding** agent and/or signal enhancing agent; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Semiconductor materials
(as signal enhancing agent; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Alloys, biological studies
Glass, biological studies
Metals, biological studies
Organic compounds, biological studies
Polymers, biological studies
Polysaccharides, biological studies
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as signal enhancing agent; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Analysis
(biochem.; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)
IT Microscopy
(dark-field; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)
IT Particles
(detectable by light scattering and coated with analyte-**binding** agents; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)
IT Spectrometers
(flow cells; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)
IT Antibodies and **Immunoglobulins**
RL: ANT (Analyte); ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fragments, as **binding** agent and/or signal enhancing agent; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)
IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**immobilized**, to digoxigenin; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)
IT **Electric** lamps
(incandescent; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)
IT Analysis
Analytical apparatus
Biosensors
CCD cameras
Diagnosis
Drug screening
Electroluminescent devices
Environmental analysis
Evanescent wave
Fluorescent lamps
Immobilization, molecular or cellular
Lasers
Light scattering
Light sources
Microscopes
Monochromators
Pharmacology
Photodiodes
Photomultipliers
Semiconductor lasers
Surface plasmon resonance
Veterinary medicine
Waveguides
(methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with

binding entities)

IT DNA
Haptens
Oligonucleotides
Polynucleotides
RNA
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Noble **metals**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Microscopes
(near-field, scanning; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Microscopy
Scanning microscopy
(near-field; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Nanoparticles
(of gold, functionalized with biotin; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Latex
(particles, as signal enhancing agent; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Microscopy
(reflection, with crossed polarizers; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Microscopy
(reflection; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Albumins, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(serum; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT Microscopy
(total-internal-reflection; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT 58-85-5, Biotin
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**conjugates** with gold nanoparticles; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT 1672-46-4, Digoxigenin 9013-20-1, Streptavidin
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

IT 7440-57-5, Gold, biological studies
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(particles, coated with antibodies to digoxigenin; methods, device and instrument for detection of analytes using particles detectable by light scattering and coated with **binding** entities)

L44 ANSWER 5 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:101323 HCAPLUS
DOCUMENT NUMBER: 140:142167
TITLE: Porous nanostructured film sensor
INVENTOR(S): Campbell, Colin; Cunningham, Emer
PATENT ASSIGNEE(S): Ntera Limited, Ire.
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011672	A1	20040205	WO 2003-IE106	20030728 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IE 2002-623 A 20020726 <--

AB A porous nanostructured film has a sensing element and/or a signal detection element covalently **immobilized** thereon. The film may have a bimodal pore distribution comprising a combination of mesopores and macropores. The film may be a **metal** oxide material. One portion of the film may have a sensing element and another portion of the film has a signal detection element **immobilized** thereon. Porous titanium oxide films having **immobilized** antibody to hCG were used with anti-hCG monoclonal antibody-horseradish peroxidase conjugate to detect hCG.

IC ICM C12Q001-00
ICS G01N033-543

CC 9-1 (Biochemical Methods)
Section cross-reference(s): 2, 15

ST porous nanostructured film sensor; chorionic gonadotropin porous titanium oxide film **immobilized** antibody

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IgA, **immobilized**; porous nanostructured film sensor)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);

DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IgD, **immobilized**; porous nanostructured film sensor)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IgE, **immobilized**; porous nanostructured film sensor)

IT Antibodies and **Immunoglobulins**
RL: ANT (Analyte); ARG (Analytical reagent use); BSU (Biological study, unclassified); CAT (Catalyst use); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(IgG, **conjugates**, with horseradish peroxidase; porous nanostructured film sensor)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IgG, **immobilized**; porous nanostructured film sensor)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IgM, **immobilized**; porous nanostructured film sensor)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(affibodies, **immobilized**; porous nanostructured film sensor)

IT **Immobilization**, molecular or cellular
(antibody; porous nanostructured film sensor)

IT Chromophores
Dyes
(as signal detection element **immobilized** on film; porous nanostructured film sensor)

IT Porphyrins
RL: ARG (Analytical reagent use); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); USES (Uses)
(as signal detection element **immobilized** on film; porous nanostructured film sensor)

IT Affinity
(**binding** agents, **immobilized**; porous nanostructured film sensor)

IT Sensors
(**electrochem.**, spectrophotometric; porous nanostructured film sensor)

IT **Biosensors**
(enzymic, chemiluminescent; porous nanostructured film sensor)

IT Proteins
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fibrin-**binding**, **immobilized**; porous nanostructured film sensor)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fragments, **immobilized**; porous nanostructured film sensor)

IT Ligands
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**immobilized**, for drug receptors; porous nanostructured film sensor)

IT Animal tissue
Aptamers
Cell
Eubacteria
(**immobilized**; porous nanostructured film sensor)

IT Antibodies and **Immunoglobulins**
Antigens
DNA
Dopamine receptors
Enzymes, biological studies
Epidermal growth factor receptors
Oligonucleotides
Proteins
Receptors
Somatostatin receptors
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**immobilized**; porous nanostructured film sensor)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal, **conjugates**, with horseradish peroxidase; porous nanostructured film sensor)

IT **Immobilization**, molecular or cellular
(of signal detection element on portion of film; porous nanostructured film sensor)

IT **Biosensors**
Electrochemical cells
Electrodes
Films
Glass substrates
Human
Ink-jet printing
Nanocrystals
Nanoparticles
Nanostructures
Pore
Screen printing
Sensors
(porous nanostructured film sensor)

IT **Immobilization**, molecular or cellular
(protein; porous nanostructured film sensor)

IT **Metals**, uses
Plastics, uses
RL: DEV (Device component use); TEM (Technical or engineered material use); USES (Uses)
(substrates; porous nanostructured film sensor)

IT 91-64-5D, Coumarin, compds., **immobilized** 553-12-8D, Protoporphyrin IX, **immobilized** 7440-18-8D, Ruthenium, complexes, **immobilized** 20910-67-2D, 2,2'-Bipyridinium, derivs.,complex with ruthenium, **immobilized**
RL: ARG (Analytical reagent use); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); USES

(Uses)
(as signal detection element; porous nanostructured film sensor)
IT 1553-55-5, Hydroxymethyl glutaryl Co-A 9001-12-1, Collagenase 9001-66-5, Monoamine oxidase 9001-91-6, Plasminogen 9055-65-6, Prostaglandin synthase 12001-79-5, Vitamin K
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**immobilized**; porous nanostructured film sensor)
IT 9003-99-0D, Peroxidase, **conjugates** with IgG
RL: ANT (Analyte); ARG (Analytical reagent use); BSU (Biological study, unclassified); CAT (Catalyst use); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(porous nanostructured film sensor)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:80237 HCAPLUS
DOCUMENT NUMBER: 140:124853
TITLE: Multiple hybrid immunoassay
INVENTOR(S): Emerson Campbell, John Lewis; Frank, Pamela Anne; Hawkes, Meghan Elizabeth; Lobin, Shannon Reishma; Miller, Cary James; Yang, Zhen
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004018577	A1	20040129	US 2002-208560	20020729 <--
WO 2004011947	A1	20040205	WO 2003-US23483	20030729 <--

W: JP
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.: US 2002-208560 A 20020729 <--
AB The invention relates to compns. and methods for the immunoassay of an analyte of interest. The analyte is detected in an immunoassay using three or more antibodies, wherein each antibody specifically **binds** to a different epitope on the analyte. When the analyte of interest is a clin. marker for an acute disease, the detection of the analyte by immunoassay is a diagnosis of the occurrence of the disease. Microparticle capture reagents were made comprising a first capture antibody to cardiac troponin I (cTnI) (CB1), a second capture antibody (CB2) to cTnI, and CB12 microparticles comprising both CB1 and CB2. Alkaline phosphatase-labeled Fab conjugates were also made comprising EC1, EC2 or the EC12 hybrid containing both EC1 and EC2. The hybrid capture reagents and hybrid signal reagents gave superior assay performance in the detection of cTnI in whole blood samples.
IC ICM G01N033-53
ICS G01N033-537; G01N033-543
NCL 435007930
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 14, 15
IT **Electrodes**
(amperometric; multiple hybrid immunoassay using three or more

different antibodies to different epitopes on analyte)
IT **Immobilization**, molecular or cellular
(antibody; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)
IT Latex
Spheres
(beads, **conjugates** with antibody; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)
IT **Electrodes**
(**bioelectrodes**; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)
IT Microparticles
(**conjugates** with antibody; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)
IT Enzymes, biological studies
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**conjugates**, with antibodies; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)
IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugates**; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)
IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fragments; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)
IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**immobilized**; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)
IT **Biosensors**
(immunosensors; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)
IT Particles
(**metal**, as label on antibodies; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)
IT Blood analysis
Crosslinking agents
Cuvettes
Diagnosis
Epitopes
Fiber optic sensors
Field effect transistors
Human
Immunoassay
Optical waveguides
Radiation detectors
Semiconductor materials
Surface acoustic wave devices

(multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)

IT Apolipoproteins
Myoglobins
Prostate-specific antigen
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)

IT **Metals**, biological studies
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(particles, as label on antibodies; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(single chain; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)

IT 9003-53-6, Polystyrene
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(beads, **conjugates** with antibody; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)

IT 25085-34-1DP, **conjugates** with antibody
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(beads; multiple hybrid immunoassay using three or more different antibodies to different epitopes on analyte)

L44 ANSWER 7 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:291461 HCAPLUS
DOCUMENT NUMBER: 140:300010
TITLE: Development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen
INVENTOR(S): Shiga, Azusa; Nukina, Yasuyuki; Nomura, Yukio
PATENT ASSIGNEE(S): Matsushita Electric Industrial Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004108815	A2	20040408	JP 2002-268531	20020913 <--
PRIORITY APPLN. INFO.:			JP 2002-268531	20020913 <--

AB An **electrode** measuring **elec.** conductivity (or resistance) through insulative membrane (mono- or multi-layer) bearing the antigen (same as analyte antigen) labeled with ion-conducting lipophilic crown ether derivative has been used as an immunosensor. The immunosensing mechanism utilizes the competition between the free and the **immobilized** antigens over the specific insol. antibody reagent. Diffusive acid that can be trapped by the crown ether is used as an sensoring mol. in the conductometry by the **electrode** system. The conductometry is performed by applying the AC **voltage** added with DC bias. Alkyl thiol of which sulfor atom is involved in **binding** to **metal** component of the **electrode** is used as a component of the insulative membrane. An **electrode** with insulative membrane containing 1-Butane thiol and bearing antigen labeled with benzo-15-crown-5 was fabricated and a sensor system was assembled with compartments of **immobilized** reagent antibody and acid reagent. Performance of the conductometry of 17β-Estradiol by immunosensing with the fabricated **electrode** bearing 4-aminobenzo-15-crown-5 labeled 17β-estradiol was demonstrated.

IC ICM G01N027-327
ICS G01N027-416; G01N033-543

CC 9-1 (Biochemical Methods)
Section cross-reference(s): 2, 15

ST conductometric immunosensor **electrode** crown ether labeled antigen **immobilized**; competitive immunoassay crown ether labeled antigen **immobilized electrode**; estradiol competitive conductometric immunosensor crown ether labeled antigen

IT **Electrodes**
(**bioelectrodes**; development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

IT Crown ethers
RL: DEV (Device component use); USES (Uses)
(**conjugates** with antigen; development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

IT Conductometry
(development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

IT **Antigens**
RL: ANT (Analyte); ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(free (analyte) or **conjugates** with crown ether (reagent); development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

IT **Biosensors**
(immunosensors; development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(insol. form, included as **immobilized** form in device; development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

IT Thiols (organic), uses
RL: DEV (Device component use); USES (Uses)
(used as insulative membrane component, **immobilized** to **electrode**; development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

IT 14098-44-3D, Benzo-15-crown-5, **conjugates** with antigen
60835-71-4D, 4-Aminobenzo-15-crown-5, **conjugates** with

17β-estradiol
RL: DEV (Device component use); USES (Uses)
(development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

IT 50-28-2D, 17β-Estradiol, **conjugates** with 4-aminobenzo-15-crown-5
RL: ANT (Analyte); ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(free (analyte) and **conjugates** (reagent); development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

IT 7647-01-0, Hydrochloric acid, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(used as diffusive acid reagent; development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

IT 109-79-5, 1-Butane thiol
RL: DEV (Device component use); USES (Uses)
(used as insulative membrane component; development of highly sensitive conductometric immunosensor **electrode** bearing crown-ether labeled antigen)

L44 ANSWER 8 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:289728 HCAPLUS
DOCUMENT NUMBER: 140:300004
TITLE: Development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring molecule
INVENTOR(S): Nukina, Yasuyuki; Nomura, Yukio; Shiga, Azusa
PATENT ASSIGNEE(S): Matsushita Electric Industrial Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004108814	A2	20040408	JP 2002-268530	20020913 <--

PRIORITY APPLN. INFO.: JP 2002-268530 20020913 <--

AB An immunosensor **electrode** using lipophilic ion conductive substances as sensoring mol. has been developed. The sensor system contains a working **metal electrode** coated with lipid thin film (mono- or multi-layer) and a counter **electrode** and reagents including soluble monoclonal antibody labeled with lipophilic ion conductive substance, insol. antibody with specificity for different epitope, and reagent antigen. Analyte antibody is designed to be trapped by labeled-antigen reagent and the formed immune-complex is deposited on the lipid thin film of the **electrode** to decrease membrane resistance, while excess antigen is removed by the insol. antibody. Lipophilic ion conductive substances that can be used in the sensor system included lipophilic chelates, lipophilic ions, amphipathic polymers, etc. The lipid thin film (mono- or multi-layer) is **bound** to the **metal electrode** via its sulfor atom and of which surface is having hydroforbic, non-ionic hydrophilic, anionic, cationic or amphoteric group. Conductometry in the sensor system is achieved by applying AC **voltage** with adding DC bias. **Electrode** fabrication by using specific components, i.e., lipophilic ion conductive substances such as aminobenzo-15 crown-5 and porphyrin and lipid films

containing specific components such as 6-amino-hexanethiol was described.
IC ICM G01N027-327
ICS G01N027-12; G01N027-416; G01N033-483; G01N033-53
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 15
ST antibody detection immunosensor conductometric **electrode** lipophilic ion conductive marker
IT Surfactants
(as lipophilic ion conductive substance labeling antibody; development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring mol.)
IT **Electrodes**
(**bioelectrodes**; development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring mol.)
IT Conductometry
(development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring mol.)
IT Antibodies and **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring mol.)
IT **Antigens**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring mol.)
IT **Biosensors**
(immunosensors; development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring mol.)
IT Chelates
RL: DEV (Device component use); USES (Uses)
(lipophilic, as lipophilic ion conductive substance labeling antibody; development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring mol.)
IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(monoclonal, **conjugates** with lipophilic ion conductive substance; development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring mol.)
IT 67283-39-0, 6-Amino hexanethiol
RL: DEV (Device component use); USES (Uses)
(used as component of lipid thin film; development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring mol.)
IT 101-60-0D, Porphyrin, **conjugates** with monoclonal antibody
60835-71-4D, 4-Aminobenzo-15 crown-5, **conjugates** with monoclonal antibody
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(used as lipophilic ion conductive substance; development of antibody-detecting conductometric immunosensor **electrode** using lipophilic ion conductive substance as sensoring mol.)

L44 ANSWER 9 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-593540 [57] WPIX

DOC. NO. NON-CPI: N2004-469411
DOC. NO. CPI: C2004-215929
TITLE: Coupling disulfide bridge containing protein or peptide to carrier, useful in enzyme assays, by irradiating protein to create thiol group in protein by disulfide bridge disruption, and incubating irradiated protein with carrier.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): DA CRUZ AUGUSTO NEVES, PETERSEN; PETERSEN, S B
PATENT ASSIGNEE(S): (BION-N) BIONANOPHOTONICS AS
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004065928	A2	20040805	(200457)*	EN	69

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004065928	A2	WO 2004-DK47	20040122

PRIORITY APPLN. INFO: US 2003-441975P 20030122; DK 2003-81 20030122
AN 2004-593540 [57] WPIX
AB WO2004065928 A UPAB: 20040907
NOVELTY - Coupling (M1) a disulfide bridge containing protein or peptide to carrier, involves irradiating protein or peptide to create a thiol group in protein or peptide by disulfide bridge disruption, and incubating the irradiated protein or peptide with a carrier capable of **binding** a thiol group, thus obtaining the coupling.

DETAILED DESCRIPTION - Coupling (M1) a disulfide bridge containing protein or peptide to carrier, involves:

(a) irradiating protein or peptide to create a thiol group in protein or peptide by disulfide bridge disruption, and incubating the irradiated protein or peptide with a carrier capable of **binding** a thiol group, thus obtaining the coupling; or

(b) incubating protein or peptide with carrier capable of **binding** a thiol group, and irradiating protein or peptide in the presence of the carrier to create a thiol group protein or peptide by disulfide bridge disruption, and thus obtaining a coupling.

INDEPENDENT CLAIMS are also included for:

(1) a carrier (I) comprising one or more protein or peptide coupled by using (M1); and

(2) predicting (M2) disulfide bridge containing protein or peptide capable of disruption by irradiation, involves:

(a) identifying and selecting a disulfide bridge containing protein or peptide;

(b) identifying and selecting protein or peptide that further comprises an aromatic amino acid residue within 10 Angstrom of the disulfide bridge, from protein or peptide identified in step (a); and

(c) identifying and selecting protein or peptide in which the plane of the dipole of the side-chain of the aromatic amino acid is not orthogonal to the plane of the disulfide bridge, from protein or peptide identified in step (b).

USE - (M1) is useful for coupling a disulfide bridge containing protein or peptide to a carrier. (I) is useful for carrying out bio-functional reactions. The bio-functional reactions are chosen from bio-sensor, chromatography, immunodetection, enzyme assay, nucleotide **binding** detection, protein-protein interaction, protein modification, carrier targeting and protein targeting. (I) is useful for the production of a bio-sensor or protein/peptide microarray, and is useful in a diagnostic or biosensor kit (claimed). (M1) is useful for obtaining (I) comprising one or more proteins or peptides coupled to it. (M1) is useful in coupling the pharmaceutical drugs to the carrier molecule, thus facilitating their effective delivery, where the stability of the drug is improved by the carrier.

ADVANTAGE - (M1) enables cost-effective and rapid method of coupling the disulfide bridge containing protein or peptide to a carrier, where the native structural and functional properties of the coupled protein or peptide are preserved, and is a single step process. The orientation of the **immobilized** protein can be controlled in a uniform and reproducible manner.

DESCRIPTION OF DRAWING(S) - The figure shows the coupling reaction between an SH group of a protein and an SS group 5'5-dithiobis(2-nitrobenzoic acid) and the stoichiometric release of nitrothiobenzoate.
Dwg.2/17

L44 ANSWER 10 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-452724 [43] WPIX
DOC. NO. NON-CPI: N2004-358407
DOC. NO. CPI: C2004-169504
TITLE: Miniature device for detecting ligand-receptor interactions, useful e.g. for diagnosis and high throughput screening, comprises solid support carrying array of pairs of nano-electrodes.
DERWENT CLASS: B04 D16 S03 U12
INVENTOR(S): DESMET, R; EL MAHDI, O; HAGUET, V; MARTIN, D; MELNYK, O; OLIVIER, C; STIEVENARD, D
PATENT ASSIGNEE(S): (CNRS) CNRS CENT NAT RECH SCI
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
FR 2847983	A1	20040604	(200443)*		32

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
FR 2847983	A1	FR 2002-15028	20021129

PRIORITY APPLN. INFO: FR 2002-15028 20021129
AN 2004-452724 [43] WPIX
AB FR 2847983 A UPAB: 20040709
NOVELTY - A miniature device (A) for electrical detection of ligand-receptor interactions comprising a solid support (S), electrically insulating, with a flat surface and carrying a matrix of nano-electrodes (NE), arranged in pairs, is new.

DETAILED DESCRIPTION - A miniature device (A) for electrical detection of ligand-receptor interactions comprises a solid support (S), electrically insulating, with a flat surface and carrying a matrix of nano-electrodes (NE), arranged in pairs. The maximum distance between NE of a pair is 1 micron and the inter-electrode space (IES) is covered with an organic hydrophilic layer (A) for fixation of polypeptide probes (PP), covalently or by adsorption. (A) is in contact with NE and the device is connected to a system for measuring the electrical conductivity between each pair of NE.

INDEPENDENT CLAIMS are also included for:

(1) a method for preparing (A); and

(2) a method for electrical detection of ligand-receptor interactions using (A).

USE - (A) is especially a polypeptide chip for:

(a) miniaturized and highly parallel diagnosis;

(b) serotyping and screening for epitopes;

(c) detection and/or quantitation of proteins in complex media, e.g. receptors or antibodies specific for the probes; and

(d) high throughput screening of peptides in complex media.

ADVANTAGE - (A) provide simple, miniaturized and inexpensive determination of specific interaction of peptides in biological media.

Dwg.0/5

L44 ANSWER 11 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2004-05279 BIOTECHDS
TITLE: Detection of pathological conditions in biological objects comprises forming an immunocomplex comprising an **antigen**, an **antibody** and a **metal**-labeled nonimmune protein on the surface of a thick-film graphite electrode; **antigen**, **antibody** or protein **immobilization** on electrode surface support for biosensor construction
AUTHOR: BRAININA H Z; IVANOVA A V; SHARAFUTDINOVA E N; RUBTSOVA M Y; KOZITSINA A N; SERGEEV B M
PATENT ASSIGNEE: UNIV URALS ECONOMICS; IVA SCI PRODN CO LTD
PATENT INFO: WO 2003105660 24 Dec 2003
APPLICATION INFO: WO 2003-RU379 17 Jun 2003
PRIORITY INFO: RU 2002-116051 **18 Jun 2002**; RU 2002-116051 18 Jun 2002
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable RS
OTHER SOURCE: WPI: 2004-071478 [07]
AN 2004-05279 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Detection of pathological conditions in biological objects comprises forming an immunocomplex comprising an **antigen**, an **antibody** and a **metal**-labeled nonimmune protein on the surface of a thick-film graphite electrode and assessing the pathological condition on the basis of a **metal** oxidation reaction.

USE - The method is especially useful for disease diagnosis.

ADVANTAGE - Use of expensive goose anti-human immunoglobulins is avoided (compare Bioelectrochem. Bioenergetics, 38, 389, 1995).

EXAMPLE - A thick-film graphite electrode coated with **antigen** (tick encephalitis virus) was incubated in patient serum at 37degrees C for 30 minutes, washed with buffer containing normal equine serum and Tween 20, incubated with gold-labeled protein A, washed again, and placed in a three-electrode cell containing a glassy carbon auxiliary electrode, a silver/silver chloride reference electrode and a 0.1 M hydrochloric acid electrolyte. A signal was recorded by anodic

voltamperometry at a gold oxidation potential of 1 V. The measurements were performed using a potentiostat. A control experiment was performed using serum containing no **antibodies** to tick encephalitis virus. The scanning rate was 100 mV/second. The patient serum was found to contain **antibodies** to tick encephalitis virus in an amount of 0.002 mg/ml. (18 pages)

L44 ANSWER 12 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-13189 BIOTECHDS
TITLE: Nucleic acid sensor molecule, for identifying/detecting protein kinase in a sample, comprises a target modulation domain which recognizes a target molecule, a linker domain, a catalytic domain, and an optical signal generator;
DNA biosensor for protein-kinase detection and identification
AUTHOR: STANTON M; EPSTEIN D; HAMAGUCHI N; KURZ M; KEEFE T; WILSON C; GRATE D; MARSHALL K A; MCCAULEY T; KURZ J
PATENT ASSIGNEE: ARCHEMIX CORP
PATENT INFO: WO 2003014375 20 Feb 2003
APPLICATION INFO: WO 2002-US25319 9 Aug 2002
PRIORITY INFO: US 2002-385097 **31 May 2002**; US 2001-311378 9 Aug 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-300534 [29]
AN 2003-13189 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A nucleic acid sensor molecule (I), comprises a target modulation domain that recognizes a target molecule (TM), a linker domain, a catalytic domain, and an optical signal generating unit.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a composition (C) comprising (I) and a carrier, tissue extract, cell extract or an in vitro cell culture, and optionally affixed to a substrate; (2) a system (II) for detecting a TM, comprising (I) and a detector in communication with the composition, where the detector detects changes in the optical properties of the composition; and (3) a diagnostic system (III) for identifying or detecting TM, comprising (I) and a detector in communication with (I), where the detector detects changes in the signal generated by the optical signal generating unit of the nucleic acid sensor.

WIDER DISCLOSURE - Also disclosed are: (1) reagents for generating and using (I); (2) kits having standardized reagents for making and/or using (I); (3) a computer program product comprising stored data relating to optical signal generated by profiling and/or pathway target molecules; (4) a device to compare the data to another optical signal; (5) direct mechanistic assays; (6) identifying (I); and (7) nucleic acid sensor molecules detected by (6).

BIOTECHNOLOGY - Preferred Sensor Molecule: The optical signal generating unit includes one or two signaling groups. The two (first and second) signaling groups change proximity to fluorescent quencher and recognition of a target by target modulation domain (TMD) results in an increase in detectable fluorescence of the fluorescent donor. The signaling groups comprise fluorescent energy transfer (FRET) donor and acceptor groups, and recognition of a target by TMD results in a change in distance between the donor and acceptor groups, thus changing optical properties of the molecule. The optical signal generating unit consists essentially of a first signaling group which changes conformation upon recognition of a target by TMD, thus resulting in a detectable optical signal. The nucleic acid sensor molecule includes a modified nucleic acid, and the catalytic domain comprises an endonucleolytic ribozyme

which is cis-endonucleolytic ribozyme or trans-endonucleolytic ribozyme. The endonucleolytic ribozyme is a hammerhead ribozyme. The catalytic domain comprises a self-ligating ribozyme which is cis-ligase ribozyme or trans-ligase ribozyme, particularly a 1-piece ligase, 2-piece ligase or 3-piece ligase. The 1-piece ligase ribozyme comprises TMD that recognizes a target, linker domain, and catalytic domain, where the 5' and 3' ends of the ligase ligate to each other upon recognition of the target by the modulation domain. The 2-piece ligase ribozyme comprises TMD that recognizes a target, linker domain, and catalytic domain comprising an oligonucleotide super substrate **binding** domain, where upon recognition of the target by the modulation domain, the 3' end of the oligonucleotide super substrate is ligated on the 5' end of the oligonucleotide substrate ligation site. The 3-piece ligase ribozyme comprises TMD that recognizes a target, linker domain, catalytic domain comprising an oligonucleotide substrate **binding** domain and an effector-oligonucleotide **binding** site, where upon recognition of the target by the modulation domain, and in the presence of **binding** of the effector oligonucleotide to the effector-oligonucleotide **binding** site, then the 3' end of the oligonucleotide substrate is ligated to the 5' end of the ligase. (I) Comprises a catalytic domain that comprises a ligase or cis-hammerhead, and the linker domain links TMD and catalytic domain. (I) Comprises a non-radioactive detectable label. Preferred Composition: (C) Further comprising an RNase inhibitor. (C) Is RNase-free. The substrate is glass, gold or other **metal**, silicon or other semi-conductor material, nitrocellulose, nylon or plastic. (I) Is covalently or non-covalently attached to the substrate. The substrate comprises 50, 250 or 500 nucleic acid sensor molecules. Preferred System: (II) Further comprises a light source in optical communication with the composition and a processor for processing optical signals detected by the detector. The system comprises several nucleic acid sensor molecules, where two of the biosensor molecules each recognize different TM.

USE - (I) Is useful for identifying or detecting TM in a sample, preferably a protein kinase in a sample. Target molecules include proteins, post-translationally modified forms of proteins, peptides, nucleic acids, oligosaccharides, nucleotides, metabolites, drugs, toxins, biohazards, ions, carbohydrates, polysaccharides, hormones, receptors, **antigens**, **antibodies**, viruses, metabolites, co-factors, drugs, dyes, nutrients, growth factors, cCMP, cAMP or cGMP, protein kinase, phosphorylated protein kinase, extracellular signal regulated kinase (ERK), a component or product of mitogen activated protein (MAP) kinase pathway, a MAP kinase pathway associated protein, an extracellular component of MAP kinase pathway, a component of ERK1/2 MAP, JNK MAP or P38 MAP kinase pathway, an endogenous form of MAP kinase (MEK), MAP kinase kinase, or MAP kinase (MEKKK), or RAF kinase, Ras protein, phosphatase, GTP **binding** protein, G-protein coupled receptor (GPCR), cytokine, growth factor, cellular metabolite, small molecule or lysozyme. (I) Is useful for identifying a modulator of protein kinase activity (claimed). (I) Is useful for monitoring the presence or concentration of various TM, in solution-based homogeneous assays, in homogeneous intracellular assays, in heterogeneous assays, in drug discovery, including target validation and discovery and development, high throughput screening, in biochemical assay, and in in vitro cellular models and in vivo animal models. (I) Is also useful in diagnostic assays, for detection of conformational isoforms of G-protein coupled receptors, as a screening tool in assays designed to detect agonists of the beta-2 adrenergic receptor, to monitor the response of single elements of a pathway, and to quantify the level and chemical state of all components in a molecular pathway. (I) Is useful in drug optimization, medicinal chemistry, pharmacokinetic studies, chemical

genomic assays, in clinical trials to determined the fate of drugs and in TM separation.

ADVANTAGE - (I) Function in formats where the target analytes are present in complex biological mixtures, or the assays are themselves performed in multiplexed formats.

EXAMPLE - Nucleic acid sensor molecules (NASMs) were generated from pools of ribozymes comprised of randomized linker and target modulation domains. Target modulated nucleic acid sensor molecules were isolated by in vitro selection. Pools of partially randomized ribozymes with 1015 - 1017 unique sequences were used for in vitro selection. The L1 ligase and hammerhead ribozyme were used as platforms for the selection of allosterically-controlled molecules. Selections were designed to yield ribozymes that specifically respond to any target. Nucleic acid sensor molecules with cross-specificity were selected against by including the undesired from of the target in an initial negative selection step. The starting library of DNA sequences were generated by automated chemical synthesis on DNA synthesizer. This library of sequences were transcribed in vitro into RNA using T7 RNA polymerase, purified, and captured onto beads using an oligonucleotide tag complementary to the 3'-end. In the absence of the desired modulator (target), the RNA library were incubated together with the undesired form of the modulator and an arbitrary sequence oligonucleotide substrate (substrate 1). The undesired form of the modulator and oligonucleotide substrate 1 were removed by washing. The **immobilized** RNA pool was then incubated under identical conditions in the presence of the intended modulator and a second biotinylated oligonucleotide substrate (substrate 2). Ligases active only in the presence of the desired modulator were isolated using streptavidin capture and selective polymerase chain reaction (PCR) amplification. Hammerheads active only in the presence of the desired modulator were isolated by gel electrophoresis. PCR amplified DNA were purified and transcribed to yield an enriched pool for subsequent reselection. Rounds of selection an amplification were repeated until functional members sufficiently dominate the resultant library. Nucleic acid sensor molecules which were derived from in vitro selection were tested as target modulated biosensors. The pool of NASMs were cloned into various plasmids that contain a T7 promoter transformed into Escherichia coli. Individual NASM encoded DNA clones were isolated, linearized and the NASM was transcribed in vitro to generated NASM RNA. The NASM RNAs were then tested in target modulation assays which determine the rate or extent of ribozyme modulation. For hammerhead NASNs, the extent of target dependent and independent reaction was determined by quantifying the extent of endonucleolytic cleavage of an oligonucleotide substrate. The extent of reaction was followed by electrophoresing the reaction products on a denaturing polyacrylamide gel electrophoresis (PAGE) gel, and subsequently analyzed by standard radiometric method. For Ligase NASMs, the extent of target dependent and independent reaction was determined by quantifying the extent of ligation of an oligonucleotide substrate, resulting in an increase in NASM molecular weight, as determined in denaturing PAGE gel electrophoresis. Individual NASM clones which display high target dependent switch factor values, or high Kact rate values were subsequently chosen for further modification and evaluation. Hammerhead derived NASM clones were then further modified to render them suitable for the optical detection applications. These NASMs were used as fluorescent biosensors affixed to solid supports, as fluorescent biosensors in homogeneous fluorescent energy transfer (FRET)-based assays. (423 pages)

L44 ANSWER 13 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2004-10868 BIOTECHDS
TITLE: Biosensor for detecting bacteria, fungi, virus, has substrate

with a pattern of active areas of receptive material and pattern of blocking material areas, the receptive material being specific for analyte of interest;
DNA or protein for biosensor construction

AUTHOR: COHEN D; KAYLOR R
PATENT ASSIGNEE: COHEN D; KAYLOR R
PATENT INFO: US 2003207258 6 Nov 2003
APPLICATION INFO: US 2002-139025 3 May 2002
PRIORITY INFO: US 2002-139025 **3 May 2002**; US 2002-139025 3 May 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-166976 [16]
AN 2004-10868 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A biosensor (I) comprises substrate (S) with a pattern of active areas of receptive material and pattern of blocking material areas. The receptive material and blocking material are attached to (S) with the photo-reactive cross-linking agent activated in a masking process, and where the receptive material is specific for an analyte of interest.

DETAILED DESCRIPTION - A biosensor (I), comprising a substrate (S) (4); a layer containing a photo-reactive cross-linking agent (Ia) (2) applied to (S); a pattern of active receptive material (Ib) (6) areas defined on (S) by attachment with (Ia), where (Ia) comprises molecules specific for an analyte of interest (II); a pattern of inactive blocking material (Ic) (16) areas defined in (S) by attachment with (Ia), where (Ic) areas are interposed with (Ib) areas and are non-reactive with (II); where (Ib) and (Ic) areas are defined on (S) by a masking process, in which a mask (8) is placed over (S) prior to irradiating (S) with an energy source (14) sufficient for activating (Ia) such that areas exposed by the mask define one of (Ib) and (Ic) areas, and the areas shield by the mask defined the other of (Ic) and (Ib) areas; and where when (I) is exposed to a medium containing (II), the analyte **binds** to (Ib) in the active areas and subsequently facilitate diffraction of transmitted or reflected light in a diffraction pattern corresponding to (Ib) areas. An INDEPENDENT CLAIM is also included for making a biosensor, involves applying (Ia) to a surface of (S), forming one of a (Ib) layer and a (Ic) layer over (Ia), placing a mask over (S), the mask having a configuration so as to shield at least one underlying area of (S) while exposing at least one adjacent area, and irradiating (S) and mask combination with an energy source sufficient to activate (Ia) in the areas exposed by the mask, the activated (Ia) cross-linking with the respective (Ib) or (Ic) in the exposed areas; cleaning the unreacted (Ib) or (Ic) from the shielded areas of (S) after removal of the mask, forming a layer of the respective other of (Ic) and (Ib) over the surface of (S), and irradiating (S) with the energy source so as to activate the remaining (Ia) in the previously shielded areas, the activated (Ia) cross-linking with the respective (Ic) or (Ib), and where a resulting pattern of (Ib) and (Ic) areas are defined according to the pattern of shielded and exposed areas of the mask.

BIOTECHNOLOGY - Preferred Biosensor: (S) comprises a material chosen from plastics, **metal** coated plastics and glass, functionalized plastics and glass, silicon wafers, glass and foils. (S) comprises a polymer film (e.g., polyethylene-terephthalate) coated with a **metal** chosen from gold, silver, chromium, nickel, platinum, aluminum, iron, copper, gold, oxide, chromium oxide, titanium, titanium oxide, silicone nitride, silver oxide, or zirconium. The diffraction pattern in visible to the naked eye. The receptive material is protein-based and is preferably an **antibody.** (S) is irradiated

with UV light at a wavelength sufficient for activating (Ia) exposed through the mask. (Ib) is at least one of **antigens**, **antibodies**, nucleotides, chelators, enzymes, bacteria, yeasts, fungi, viruses, bacterial pili, bacterial flagellar materials, nucleic acids, polysaccharides, lipids, proteins, carbohydrates, **metals**, hormones, peptides, aptamers and respective receptors for the materials. (Ia) comprises one of SANPAH (N-Succinimidyl 2-(p-azidosalicylamido)ethyl-1,3'-dithiopropionate); SAND (Sulfosuccinimidyl 2-(m-azido-o-nitro-benzamido) ethyl-1, 3'-dithiopropionate); and ANB-NOS (N-5-Azido-2-nitrobenzoyloxysuccinimide). (Ic) comprises a material that is non-reactive with (II). The pattern of (Ib) areas corresponds to the exposed areas of the mask, and the pattern of (Ic) areas corresponds to the shielded areas of the mask. Preferred Method: The method comprises forming (Ib) layer on (S) before (Ic) layer such that the pattern of active areas of receptive correspond to the exposed areas of the mask. The method comprises irradiating (S) with UV light at a wavelength sufficient for activating (Ia) exposed to the mask.

USE - (I) is useful for detecting (II) such as bacteria, yeast, fungus, virus, rheumatoid factor, IgG, IgM, IgA, IgD and IgE **antibodies**, carcinoembryonic **antigen**, Streptococcus Group A **antigen**, viral **antigens**, **antigens** associated with autoimmune disease, allergens, tumor **antigens**, Streptococcus group B **antigen**, HIV I or HIV II **antigen**, **antibodies** to viruses, **antigens** specific to Rous sarcoma virus (RSV), an **antibody**, **antigen**, enzyme, hormone, polysaccharide, protein, lipid, carbohydrate, drug, nucleic acid, Neisseria meningitidis group A, B, C, Y and W sub 135, Streptococcus pneumoniae, Escherichia coli K1, Haemophilus influenza type A/B, an **antigen** derived from microorganisms, prostate specific **antigen** (PSA) and C-reactive protein (CRP) **antigens**, a hapten, a drug of abuse, a therapeutic drug, an environmental agent, or **antigens** specific to Hepatitis (claimed). (I) is used in the detection of chemical or biological contamination in garments,such as diapers, the detection of contamination by microorganisms in prepacked foods such as meats, fruit juices or other beverages, and in health diagnostic applications such as diagnostic kits for the detection or protein, hormones, **antigens**, nucleic acids, microorganisms, and blood constituents. (I) can also be used on contact lenses, eyeglasses, window panes, pharmaceutical vials, solvent containers, water bottles, band-aids, wipes, etc., to detect contamination.

ADVANTAGE - (I) can be mass produced at a low cost, and is disposable. (I) is capable of reliable and sensitive detection of analytes, and avoids possible drawbacks of conventional microcontact printing techniques. (9 pages)

L44 ANSWER 14 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2004-10867 BIOTECHDS
TITLE: Biosensor useful for detecting presence of analyte e.g., fungi in medium comprises substrate material, receptive material layer covering substrate material and pattern of active, inactive regions of receptive material; DNA or protein for biosensor construction
AUTHOR: KAYLOR R; COHEN D
PATENT ASSIGNEE: KAYLOR R; COHEN D
PATENT INFO: US 2003207253 6 Nov 2003
APPLICATION INFO: US 2002-138598 3 May 2002
PRIORITY INFO: US 2002-138598 **3 May 2002**; US 2002-138598 3 May 2002
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: WPI: 2004-166975 [16]
AN 2004-10867 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A biosensor (I) comprises substrate material (II), receptive material layer (III) covering side of (II), receptive material being specific for analyte of interest, pattern of active and inactive regions formed by masking processing where mask is placed over (II) such that regions exposed and protected by mask define pattern of inactive and active regions of receptive material respectively.

DETAILED DESCRIPTION - A biosensor (I) comprises substrate material (4) (II), receptive material layer (2) (III) generally uniformly covering side of (II), receptive material being specific for analyte of interest, pattern of active and inactive regions formed by masking processing where mask (6) is placed over (II) such that regions exposed and protected by mask define the pattern of inactive and active regions (14) of receptive material respectively. When (I) is exposed to a medium containing the analyte of interest, the analyte **binds** to receptive material in active regions and subsequently facilitate diffraction of transmitted or reflected light in a diffraction pattern corresponding to active regions. An INDEPENDENT CLAIM is also included for making (M1) (I) which involves forming (III) generally uniformly over a surface of (II), the layer containing a receptive material specific for an analyte of interest, placing a mask over (II), the mask having a configuration so as to cover an underlying region of (II) while exposing an adjacent region, irradiating (III) and mask in combination with an energy source sufficient to deactivate the receptive material regions exposed by the mask, removing the mask from (II), and where a resulting pattern of active and inactive regions of the receptive material are defined, the inactive regions corresponding to the regions exposed by the mask and the active regions corresponding to the regions underlying the mask such that when (I) is exposed to medium containing the analyte of interest, the analyte **binds** to the receptive material in the active regions and subsequently facilitates diffraction of transmitted or reflected light in a diffraction pattern corresponding to the active region.

BIOTECHNOLOGY - Preferred Biosensor: In (I), the inactive regions of receptive material are irradiated with an energy source through the mask in the masking process. The substrate comprises a material chosen from materials consisting of plastics, **metal** coated plastics and glass, functionalized plastics and glass, silicon wafers, glass and foils, polymer film coated with a **metal** where polymer film comprises polyethylene-terephthalate. The **metal** is chosen from gold, silver, chromium, nickel, platinum, aluminum, iron, copper, titanium, gold oxide, chromium oxide, silver oxide, or zirconium preferably gold. The diffraction pattern is visible to the naked eye. The receptive material is protein based preferably an **antibody.** (II) is irradiated with UV light at a wavelength sufficient for deactivating receptive material exposed through the mask. The receptive material is chosen from **antigens**, **antibodies**, nucleotides, chelators, enzymes, bacteria, yeasts, fungi, viruses, bacterial pili, bacterial flagellar materials, nucleic acids, polysaccharides, lipids, proteins, carbohydrates, **metals**, hormones, aptamers, peptides, and respective receptors for materials. Preferred Method: (M1) further involves depositing the gold coating onto the polymer film at a thickness of 1-1000 nm, viewing the diffraction pattern of active regions with the naked eye and defining several opening (10) through the mask in a desired pattern, the openings defining the pattern of inactive regions.

USE - (I) is useful for detecting the presence of analyte such as bacteria, yeast, fungus, virus, rheumatoid factor, IgG, IgM, IgA, IgD,

and IgE **antibodies**, carcinoembryonic **antigen**, Streptococcus Group A **antigen**, viral **antigens**, **antigens** associated with autoimmune disease, allergens, tumor **antigens**, Streptococcus group B **antigen**, HIV or HIV II **antigen**, **antibodies** viruses, **antigens** specific to RSV, an **antibody**, **antigen**, enzyme, hormone, polysaccharide, protein, lipid, carbohydrate, drug, nucleic acid, Neisseria meningitides groups A, B, C, Y and W sub 135, Streptococcus pneumoniae, Escherichia coli K1, Haemophilus influenza type A/B, an **antigen** derived from microorganisms, PSA and CRP **antigens**, a hapten, a drug of abuse, a therapeutic drug, an environmental agent, or **antigens** specific to Hepatitis, in a medium (claimed).

ADVANTAGE - (I) is inexpensive and highly sensitive in detecting analytes. (10 pages)

L44 ANSWER 15 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-23977 BIOTECHDS
TITLE: Biosensor surface for detecting biological materials, has polymer derivative containing poly(ethylene glycol) segment fixed by coupling formed via trialkoxy silyl portion of derivative;
surface support for biosensor or DNA biosensor construction
PATENT ASSIGNEE: SENTAN KAGAKU GIJUTSU INCUBATION CENT KK
PATENT INFO: JP 2003149245 21 May 2003
APPLICATION INFO: JP 2001-344375 9 Nov 2001
PRIORITY INFO: JP 2001-344375 **9 Nov 2001**; JP 2001-344375 9 Nov 2001
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2003-666952 [63]
AN 2003-23977 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A biosensor surface has a polymer derivative containing poly(ethylene glycol) segment (I) fixed by a coupling formed via trialkoxy silyl portion of the derivative.

DETAILED DESCRIPTION - A biosensor surface has a polymer derivative containing poly(ethylene glycol) segment of formula (R1O)(R2O)(R3O)Si-(CH2)p-L1-(A)m(OCH2CH2)n-OL2-B (I) fixed by a coupling formed via trialkoxy silyl portion of the derivative. R1-R3 = lower alkyl; L1 = connecting group or valence bond; A = -OCHRaC(O)OCHRaC(O)- or -O(CH2)qC(O)-; L2 = connecting group; B = functional group or ligand: p = 2-5; m = 0 or 1-1000; n = 10-20000; Ra = H or lower alkyl; and q = 2-5. An INDEPENDENT CLAIM is also included for the preparation of biosensor surface which involves contacting material in a polymer derivative containing poly(ethylene glycol) segment in the presence of a solvent, removing solvent, drying, optionally detaching protecting group, and coupling **binding** partner which can couple specifically to the polymer terminal.

USE - For detecting biological materials such as **antigen**, **antibody**, lectin, saccharides, receptor protein and polynucleotide.

ADVANTAGE - The biosensor surface effectively suppresses non-specific adsorption of proteins, and detects specific reaction between ligand receptor even in the presence of contaminated proteins.

EXAMPLE - Tetrahydrofuran (THF; 30 ml), 2,2,5,5-tetramethyl-2,5-disila-1-azacyclo pentane (1 mmol), THF solution of potassium naphthalene (1 mmol) and ethylene oxide (100 mmol) were mixed. Polymerization was performed for 2 days and 3-triethoxy silylpropyl

isocyanate (1 mmol) was added. The reaction was performed for 1 hour and acetic acid was added in drops. The mixture was extracted in chloroform, washed with saturated salt solution and the organic phase was dehydrated with anhydrous sodium sulfate. A hetero bifunctional polyethylene glycol having primary amine at alpha- and alkoxy silane at omega-end, was obtained. A titanium surface was immersed in anhydrous toluene solution of the obtained alkoxy silane polyethylene glycol and the titanium surface was washed with toluene and ethanol. The surface was dried under reduced pressure at 70 degrees C for 24 hours, and a biosensor surface was prepared. (8 pages)

L44 ANSWER 16 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-27516 BIOTECHDS
TITLE: New disposable immunosensor device for detecting a target **antigen** in a fluid sample requires no wash procedures and generates no liquid waste and is useful for performing immunoassays;
antibody immobilization on support for immune biosensor construction and immunoassay
AUTHOR: HODGES A; CHATELIER R
PATENT ASSIGNEE: LIFESCAN INC
PATENT INFO: EP 1347302 24 Sep 2003
APPLICATION INFO: EP 2003-251762 20 Mar 2003
PRIORITY INFO: US 2002-105050 **21 Mar 2002**; US 2002-105050 21 Mar 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-781095 [74]
AN 2003-27516 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A disposable device for detecting a target **antigen** in a fluid comprising a reaction chamber with a fixed **immobilized antibody**, a reporter complex comprising a probe linked to a reporter complex **antigen**, where the reporter complex **antigen** is **bound** to the **antibody** but **binds** less strongly than a target **antigen**, a detection chamber, a sample ingress to the reaction chamber and a sample passageway between the reaction and detection chambers, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for determining an amount of a target **antigen** in a fluid sample, comprising: (a) placing the fluid sample in a reaction chamber containing an **immobilized antibody** and a reporter complex comprising a probe linked to a reporter complex **antigen**, where the reporter complex **antigen** is **bound** to the **antibody** but **binds** less strongly than the target **antigen**; (b) dissociating a portion of the reporter complex **antigen** from the **immobilized antibody** into the fluid sample; (c) **binding** a portion of the target **antigen** to the **immobilized antibody** ;transferring fluid sample to a detection chamber; and (d) determining an amount of reporter complex in the fluid sample, where the amount of reporter complex indicates initial amount of target **antigen** in the sample
BIOTECHNOLOGY - Preferred Device: The reporter complex **antigen** may be the target **antigen**, a psuedo-**antigen** or a modified **antigen.** The probe may be a radioisotope, fluorophore, chromophore or enzyme. Where the probe is an enzyme the device further comprises an enzyme substrate particularly an oxidizable enzyme substrate, supported on an interior surface of the detection chamber. Most preferably the enzyme is glucose dehydrogenase

and the substrate is glucose. The device preferably further comprises a mediator, particularly dichlorophenolindophenol, a complex between a transition **metal** and a nitrogen-containing heteroatomic species or ferricyanide. The preferred device also comprises a buffer to adjust the sample pH, preferably a phosphate or mellitate buffer, and a stabilizer that stabilizes the target **antigen**, reporter complex **antigen**, enzyme and/or **immobilized antibody.** The **immobilized antibody** is supported on a reaction chamber interior surface. The device may comprise a support material in the detection chamber to support the enzyme substrate, mediator or buffer and in the reaction chamber to support the **immobilized antibody** the reporter complex or an agent that prevents non-specific **binding** of proteins to a reaction chamber internal surface. The support material comprises a mesh material, a fibrous filling material, a porous material, a sintered powder, a macroporous membrane or a bead. The detection chamber preferably comprises two electrodes and the detection chamber wall is transparent to a radiation emitted or absorbed by the probe, which indicates presence of the reporter complex in the detection chamber. A wall of the detection or reaction chamber may comprise a filler of titanium dioxide, carbon, silica and/or glass. A detector detects when the reaction chamber is substantially filled. The target **antigen** preferably comprises a human C-reactive protein and the reporter complex **antigen** is a monomeric C-reactive protein, a C-reactive protein derived from a non-human species or a chemically modified C-reactive protein having less affinity than the human C-reactive protein to the **antibody.** The probe may comprise an enzyme co-factor, particularly flavin mononucleotide, flavin adenine dinucleotide, nicotinamide adenine dinucleotide or pyrroloquinoline quinine, linked to the reporter complex **antigen** through a flexible spacer, and the device also comprises an apoenzyme. Alternatively the probe comprises an enzyme activity regulator particularly a kinase or phosphorylase and the device also comprises an enzyme. Or the protein comprises a protein subunit of a multisubunit enzyme. Preferred Method: Transferring the sample to the detection chamber comprises transferring it to an electrochemical cell comprising two electrodes. Determining an amount of reporter complex in the sample comprises applying a potential between the electrodes and measuring current, where the current indicates amount of reporter in the sample and amount of reporter indicates amount of target **antigen** initially in the sample. Alternatively transferring the sample to a detection chamber comprises transferring it to a detection chamber comprising an electromagnetic radiation transmissive portion. Determining amount of reporter complex comprises exposing the portion to electromagnetic radiation which passes through the sample or reflects from the sample, and monitoring a property of the radiation which indicates the amount of reporter complex in the sample and amount of reporter indicates amount of target **antigen** initially in the sample.

USE - The device is useful for performing immunoassays.

ADVANTAGE - Unlike prior art the device provides an immunoassay method which does not require any washing steps and generates no liquid waste. (19 pages)

L44 ANSWER 17 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:221926 HCAPLUS
DOCUMENT NUMBER: 138:251070
TITLE: Device with chemical surface patterns
INVENTOR(S): Textor, Marcus; Michel, Roger; Voeroes, Janos; Hubbell, Jeffrey A.; Lussi, Jost
PATENT ASSIGNEE(S): Eidgenoessische Technische Hochschule Zuerich, Switz.

SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003023401	A1	20030320	WO 2001-CH548	20010912 <--
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1425583	A1	20040609	EP 2001-960055	20010912 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: WO 2001-CH548 W 20010912 <--

AB The invention concerns a device with chemical surface patterns (defined surface areas of at least two different chemical compns.) with biochem. or biol. relevance on substrates with prefabricated patterns of at least two different types of regions (α, β,...), whereas at least two different, consecutively applied mol. self-assembly systems (A, B...) are used in a way that at least one of the applied assembly systems (A or B or...) is specific to one type of the prefabricated patterns (α or β or...). A silicon wafer was coated with TiO2 followed by SiO2 and a pattern of 5 X 5 squares of TiO2 was etched through the SiO2 layer. The patterned surface was dipped in aqueous ammonium dodecyl phosphate for self-assembly of DDP on top of the TiO2 areas, rendering these areas highly hydrophobic. The surface was dipped in an aqueous solution of poly(L-lysine)-g-poly(ethylene glycol) (PLL-g-PEG) to **selectively** adsorbed to the SiO2 regions. Texas Red-streptavidin **selectively** adsorbed to the PLL-g-PEG coating.

IC ICM G01N033-543
ICS A61L029-08; A61L027-34; A61L031-10; A61L027-28

CC 9-1 (Biochemical Methods)

ST device surface pattern biochem substrate prepattern; self assembly dodecyl phosphate titanium oxide; polylysine PEG **selective** adsorption silicon oxide; protein **selective** adsorption patterned surface

IT **Polyelectrolytes**
(cationic, copolymers, **selective** assembly on prepatterned surfaces; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT Polymers, reactions
RL: DEV (Device component use); RCT (Reactant); TEM (Technical or engineered material use); RACT (Reactant or reagent); USES (Uses)
(co-, polycationic, **selective** assembly on prepatterned surfaces; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT **Metals**, uses
RL: ARG (Analytical reagent use); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); USES (Uses)
(colloids, as labels; device with chemical surface patterns with biochems.

on substrates with prefabricated patterns)
IT Albumins, biological studies
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); BIOL (Biological study); PROC (Process)
(**conjugates** with Oregon Green, **selective** adsorption on patterned silicon wafer; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)
IT Adhesion, biological
Agrochemicals
Animal
Animal tissue culture
Apparatus
Aptamers
Bioassay
Biosensors
Blood analysis
Cell
Cell differentiation
Cell morphology
Cell proliferation
Chelating agents
Combinatorial chemistry
Cytoskeleton
Diagnosis
Diffraction gratings
Drug screening
Environmental analysis
Evanescent wave
Fluorescence microscopy
Food analysis
Human
Immobilization, molecular or cellular
Luminescent substances
Medical goods
Molecular association
Optical waveguides
Pharmaceutical analysis
Plant analysis
Soil analysis
Spin labels
Surface
Urine analysis
Veterinary medicine
(device with chemical surface patterns with biochems. on substrates with prefabricated patterns)
IT Agglutinins and Lectins
Antibodies and **Immunoglobulins**
Antigens
DNA
Enzymes, analysis
Glycopeptides
Nucleic acids
Oligonucleotides
Oligosaccharides, analysis
Peptide nucleic acids
Polynucleotides
RNA
RL: ANT (Analyte); ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered

material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fragments; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT Polymers, reactions
RL: DEV (Device component use); RCT (Reactant); TEM (Technical or engineered material use); RACT (Reactant or reagent); USES (Uses)
(graft, with PEG, **selective** coating on prepatterned surfaces by **electrostatic** interactions at specific pH; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT Polyoxyalkylenes, reactions
RL: DEV (Device component use); RCT (Reactant); TEM (Technical or engineered material use); RACT (Reactant or reagent); USES (Uses)
(grafted polymers, **selective** coating on prepatterned surfaces by **electrostatic** interactions at specific pH; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT Cell membrane
(**immobilized** peptide or protein interacting with receptors in; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**immobilized** peptide or protein interacting with, in cell membranes; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT Peptides, biological studies
Proteins
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**immobilized**; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT pH
(in **selective** coating of PEG-grafted polymers on prepatterned surfaces by **electrostatic** interactions; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT ESR (**electron** spin resonance)
NMR spectroscopy
(labels for; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT Antibodies and **Immunoglobulins**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT **Isoelectric** point
(of oxide, nitride, or carbide areas; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT Carbides
Nitrides

Oxides (inorganic), reactions
Transition **metal** oxides
RL: DEV (Device component use); RCT (Reactant); TEM (Technical or engineered material use); RACT (Reactant or reagent); USES (Uses)
(phosphate- or phosphonate-interacting prefabricated patterns of; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT **Electrostatic** deposition
(**selective**, of PEG-grafted polymers on prepatterned surfaces; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT 58-85-5D, Biotin, **conjugates**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT 151754-91-5
RL: ARU (Analytical role, unclassified); DEV (Device component use); TEM (Technical or engineered material use); ANST (Analytical study); USES (Uses)
(for blocking protein **binding** to silicon dioxide regions of silicon wafer; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT 99896-85-2D, **immobilized** 123063-31-0D, **immobilized**
134580-64-6D, **immobilized** 193613-75-1D, **immobilized**
359878-44-7D, **immobilized** 393153-52-1D, **immobilized**
502453-68-1D, **immobilized** 502453-69-2D, **immobilized**
502453-70-5D, **immobilized** 502453-71-6D, **immobilized**
502453-72-7D, **immobilized** 502453-73-8D, **immobilized**
502453-74-9D, **immobilized** 502453-75-0D, **immobilized**
502453-76-1D, **immobilized** 502453-77-2D, **immobilized**
502453-78-3D, **immobilized** 502453-79-4D, **immobilized**
502453-80-7D, **immobilized** 502453-81-8D, **immobilized**
502453-82-9D, **immobilized** 502453-83-0D, **immobilized**
502453-84-1D, **immobilized** 502453-85-2D, **immobilized**
502453-86-3D, **immobilized** 502453-87-4D, **immobilized**
502453-88-5D, **immobilized** 502453-89-6D, **immobilized**
502453-90-9D, **immobilized** 502453-91-0D, **immobilized**
502453-92-1D, **immobilized** 502453-93-2D, **immobilized**
502453-94-3D, **immobilized** 502453-95-4D, **immobilized**
502453-96-5D, **immobilized** 502453-97-6D, **immobilized**
502453-98-7D, **immobilized** 502453-99-8D, **immobilized**
502454-00-4D, **immobilized** 502454-01-5D, **immobilized**
502454-02-6D, **immobilized** 502454-03-7D, **immobilized**
502454-04-8D, **immobilized** 502454-05-9D, **immobilized**
502454-06-0D, **immobilized** 502454-07-1D, **immobilized**
502454-08-2D, **immobilized** 502454-09-3D, **immobilized**
502454-10-6D, **immobilized** 502454-11-7D, **immobilized**
502454-12-8D, **immobilized** 502454-13-9D, **immobilized**
502454-14-0D, **immobilized** 502454-15-1D, **immobilized**
502454-16-2D, **immobilized** 502454-17-3D, **immobilized**
502454-18-4D, **immobilized** 502454-19-5D, **immobilized**
502454-20-8D, **immobilized** 502454-21-9D, **immobilized**
502454-22-0D, **immobilized** 502454-23-1D, **immobilized**
502454-24-2D, **immobilized** 502454-25-3D, **immobilized**
502454-26-4D, **immobilized** 502454-27-5D, **immobilized**
502454-28-6D, **immobilized** 502454-29-7D, **immobilized**
502454-30-0D, **immobilized** 502454-31-1D, **immobilized**
502454-32-2D, **immobilized** 502454-33-3D, **immobilized**

502454-34-4D, **immobilized** 502454-35-5D, **immobilized**
502454-36-6D, **immobilized** 502454-37-7D, **immobilized**
502454-38-8D, **immobilized** 502454-39-9D, **immobilized**
502454-40-2D, **immobilized** 502454-41-3D, **immobilized**
502454-42-4D, **immobilized** 502454-43-5D, **immobilized**
502454-44-6D, **immobilized** 502454-45-7D, **immobilized**
502454-46-8D, **immobilized** 502454-47-9D, **immobilized**
502454-48-0D, **immobilized** 502454-49-1D, **immobilized**
502454-50-4D, **immobilized** 502454-51-5D, **immobilized**
502454-52-6D, **immobilized** 502454-53-7D, **immobilized**
502454-54-8D, **immobilized** 502454-55-9D, **immobilized**
502454-56-0D, **immobilized** 502454-57-1D, **immobilized**
502454-58-2D, **immobilized** 502454-59-3D, **immobilized**
502454-60-6D, **immobilized** 502454-61-7D, **immobilized**
502454-62-8D, **immobilized** 502454-63-9D, **immobilized**
502454-64-0D, **immobilized** 502454-65-1D, **immobilized**
502454-66-2D, **immobilized** 502454-67-3D, **immobilized**
502454-68-4D, **immobilized** 502454-69-5D, **immobilized**
502454-70-8D, **immobilized** 502454-71-9D, **immobilized**
502454-72-0D, **immobilized** 502454-73-1D, **immobilized**
502454-74-2D, **immobilized** 502454-75-3D, **immobilized**
502454-76-4D, **immobilized** 502454-77-5D, **immobilized**
502454-78-6D, **immobilized** 502454-79-7D, **immobilized**
502454-80-0D, **immobilized** 502454-81-1D, **immobilized**
RL: BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); TEM (Technical or engineered material use); BIOL (Biological study); USES (Uses)
(in patterns in biomed. device; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT 195136-58-4D, **conjugates** with albumin
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); BIOL (Biological study); PROC (Process)
(**selective** adsorption on patterned silicon wafer; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT 9013-20-1D, Streptavidin, **conjugates** with Texas Red
82354-19-6D, Texas Red, **conjugates** with streptavidin
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(**selective** adsorption on patterned silicon wafer; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

IT 25322-68-3D, Polyethylene glycol, grafted polymers
RL: DEV (Device component use); RCT (Reactant); TEM (Technical or engineered material use); RACT (Reactant or reagent); USES (Uses)
(**selective** coating on prepatterned surfaces by **electrostatic** interactions at specific pH; device with chemical surface patterns with biochems. on substrates with prefabricated patterns)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 18 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:735134 HCAPLUS
DOCUMENT NUMBER: 139:257670
TITLE: **Immunoelectrode** sensors using lipid-soluble ion-conductive marker molecules
INVENTOR(S): Nukina, Yasuyuki; Miyaji, Toshiaki; Shiga, Azusa

PATENT ASSIGNEE(S): Matsushita Electric Industrial Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003262601	A2	20030919	JP 2002-61430	20020307 <--

PRIORITY APPLN. INFO.: JP 2002-61430 20020307 <--

AB The **immunoelectrode** sensors for detection of antibodies in sample liqs., have soluble antigens labeled with lipid-soluble ion-conductive substances, insolubilized antibodies to the antigens, a pair of **electrodes**, and lipid thin films formed on the working **electrode.** Antibodies in sample liqs. are detected by bringing sample solns. into contact with the labeled antigens to form conjugates of the antibodies and the labeled antigens, removing unreacted labeled antigens by **binding** with insolubilized antibodies, adsorbing the antibody-labeled antigen conjugates on the lipid thin films, and measuring the lipid-soluble ion-conductive markers based on the changes in **elec** . conductivity of the lipid thin films. Estradiol **bound** to aminobenzoyl-15-crown-5 via reaction with mercaptosuccinic anhydride and 3-maleimidopropionic acid as crosslinking mols. was exemplified as a lipid-soluble ion-conductive marker mol. for detection of receptors. High-sensitivity, accurate, rapid detection is achieved.

IC ICM G01N027-12
ICS G01N027-02; G01N027-04; G01N027-327; G01N033-483; G01N033-53; G01N033-531; G01N033-543

CC 9-1 (Biochemical Methods)
Section cross-reference(s): 2, 15

ST **immunoelectrode** sensor ionic conductor antigen; antibody detection **electrode** sensor ionic conductor; estradiol receptor detection **immunoelectrode** sensor

IT **Electrodes**
(**bioelectrodes**; **immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

IT **Antigens**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**conjugates** with lipid-soluble ionic conductors; **immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

IT Immunoassay
(**immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

IT Antibodies and **Immunoglobulins**
Estrogen receptors
Ion channel
Receptors
RL: ANT (Analyte); ANST (Analytical study)
(**immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

IT **Biosensors**
(immunosensors; **immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

IT Lipids, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)

(layer formed on **metal electrode**; **immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

IT Ionic conductors
Ionophores
(lipid-soluble, antigen **conjugates**; **immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

IT Antibodies and **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(monoclonal; **immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

IT 7440-50-8, Copper, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(**electrode**; **immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

IT 50-28-2D, Estradiol, **conjugates** with ion-conductive compds.
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

IT 67283-39-0, 6-Aminohexanethiol
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(lipid monolayer formed on **metal electrode**; **immunoelectrode** sensors using lipid-soluble ionic conductive marker mols. for detection of antibodies in liqs.)

L44 ANSWER 19 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-421272 [39] WPIX
DOC. NO. NON-CPI: N2003-336520
DOC. NO. CPI: C2003-110923
TITLE: Biosensor apparatus, useful for detecting analyte in sample, comprises vent cap, vent cap isolator, cube body, waveguide, stage and valve in fluid pathway.
DERWENT CLASS: B04 C06 D16 J04 K02 S03
INVENTOR(S): GREEN, L R
PATENT ASSIGNEE(S): (PRIT-N) PRITEST INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003031562	A1	20030417	(200339)*	EN	29

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

US 6767733 B1 20040727 (200449)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003031562	A1	WO 2002-US32359	20021009
US 6767733	B1	US 2001-974089	20011010

PRIORITY APPLN. INFO: US 2001-974089 20011010
AN 2003-421272 [39] WPIX
AB WO2003031562 A UPAB: 20030619
NOVELTY - A biosensor apparatus (100) comprises a vent cap (110), a vent cap isolator, a cube body (120), a waveguide (130), a stage (140) and at least one valve in a fluid pathway.

USE - For detecting an analyte in a sample, e.g. environmental, clinical, veterinary, pathologic and medical sample. The analyte includes protein, peptide, carbohydrate, polysaccharide, glycoprotein, lipid, hormone, growth factor, cytokine, receptor, antigen, allergen, antibody, substrate, metabolite, cofactor, inhibitor, drug, pharmaceutical, nutrient, toxin, poison, explosive, pesticide, chemical warfare agent, biowarfare agent, biohazardous agent, infectious agent, prion, radioisotope, vitamin, heterocyclic aromatic compound, carcinogen, mutagen, narcotic, amphetamine, barbiturate, hallucinogen, waste product, contaminant, heavy **metal**, virus, bacterium, Salmonella, Streptococcus, Legionella, E. coli, Giardia, Cryptosporidium, Rickettsia, spore, mold, yeast, algae, amoebae, dinoflagellate, unicellular organism, pathogen and cell (all claimed).

ADVANTAGE - The apparatus is portable, reliable and sensitive biosensor apparatus. It operates as a compact, stand-alone automated unit that can reliably analyze environmental, clinical, veterinary and medical samples under adverse field conditions, with minimal sample preparation required before analysis. Further, it analyzes multiple samples for the presence of multiple analytes simultaneously.

DESCRIPTION OF DRAWING(S) - The figures show a biosensor apparatus showing a representative fluidics cube attached to a stage.

biosensor apparatus 100
vent cap 110
cube body 120
waveguide 130
stage 140
Dwg.1/17

L44 ANSWER 20 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-130830 [13] WPIX
DOC. NO. NON-CPI: N2004-104317
DOC. NO. CPI: C2004-052185
TITLE: Biosensor having **metalized** substrate member, pattern of regions of first thiolated biomolecules defined on member, pattern formed by oxidizing blocking layer, and exposing member to biomolecules to oxidized regions.
DERWENT CLASS: A89 B04 D16 J04 P42 S03 U11
INVENTOR(S): COHEN, D; KAYLOR, R
PATENT ASSIGNEE(S): (COHE-I) COHEN D; (KAYL-I) KAYLOR R; (KIMB) KIMBERLY-CLARK WORLDWIDE INC
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003207257	A1	20031106	(200413)*		11
WO 2003093495	A2	20031113	(200413)	EN	

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR

KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW

AU 2003228555 A1 20031117 (200442)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003207257	A1	US 2002-139018	20020503
WO 2003093495	A2	WO 2003-US11756	20030415
AU 2003228555	A1	AU 2003-228555	20030415

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003228555	A1 Based on	WO 2003093495

PRIORITY APPLN. INFO: US 2002-139018 20020503

AN 2004-130830 [13] WPIX

AB US2003207257 A UPAB: 20040223

NOVELTY - Biosensor (I) comprising **metalized** substrate member, pattern of regions of first thiolated biomolecules (TB) defined on substrate member, pattern formed by oxidizing blocking layer (BL) applied to substrate, where BL is exposed to oxidizing enhancing stimulus through mask, oxidizing thiol-**metal** bonds in exposed regions of BL, and exposing substrate member to TB to form at oxidized regions of BL, is new.

DETAILED DESCRIPTION - A biosensor (I) comprising a **metalized** substrate member (4), a pattern of regions of first thiolated biomolecules (14) defined on the substrate member. The pattern formed by oxidizing a blocking layer (2) previously applied to the substrate in a masking process. The blocking layer is exposed to an oxidizing enhancing stimulus through a mask (6) having a pattern of exposed regions and protected regions (10). The exposure being for sufficient time to oxidize thiol-**metal** bonds in the exposed regions of the blocking layer under the mask. The substrate member is exposed to a source of the thiolated biomolecules for a time sufficient for a layer of the thiolated biomolecules to form at the oxidized regions of the blocking layer.

An INDEPENDENT CLAIM is also included for producing (M1) biosensors, comprising:

(a) forming a blocking layer of thiol-containing molecules on a **metalized** substrate member, the thiol-containing molecules forming thiol-**metal** bonds with the **metal** surface of the substrate member;

(b) exposing the substrate member to an oxidizing enhancing stimulus through a mask having a pattern of exposed regions and protected regions, the exposure being for sufficient time to oxidize the thiol-**metal** bonds in the exposed regions of the blocking layer under the mask; and

(c) exposing the substrate member to a first source of thiolated biomolecules for a time sufficient for a layer of the first thiolated biomolecules to form at the oxidized regions of the blocking layer.

USE - (I) is useful for detecting chemical or biological contamination in garments such as diapers, detection of contamination by microorganisms in prepacked foods such as meats, fruit juices or other beverages, as kit for detecting proteins, hormones, antigens, DNA, microorganisms and blood constituents, can be used on contact lenses, eye glasses, window panes, pharmaceutical vials, solvent carriers, water bottles, bandaids, wipes to detect contamination.

ADVANTAGE - (M1) is inexpensive.

DESCRIPTION OF DRAWING(S) - The drawing shows schematic representation of a method for producing biosensors by photo-oxidation masking process.
Blocking layer 2
Substrate member 4
Mask 6
Protected regions 10
Thiolated biomolecules 14.
Dwg.1/2

L44 ANSWER 21 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-212650 [20] WPIX
DOC. NO. NON-CPI: N2004-168408
DOC. NO. CPI: C2004-084248
TITLE: Biosensor for detecting e.g. fungi or virus, comprises a substrate with a pattern of active and inactive areas of receptive material that is specific for an analyte, the active and inactive areas being formed by a masking process.
DERWENT CLASS: A89 B04 D16 E14 G06 J04 S03 U11
INVENTOR(S): COHEN, D; KAYLOR, R
PATENT ASSIGNEE(S): (COHE-I) COHEN D; (KAYL-I) KAYLOR R; (KIMB) KIMBERLY-CLARK WORLDWIDE INC
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003207255	A1	20031106	(200420)*		9
WO 2003093806	A1	20031113	(200420)	EN	
RW:	AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW				
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW				
AU 2003221968	A1	20031117	(200442)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003207255	A1	US 2002-138882	20020503
WO 2003093806	A1	WO 2003-US11758	20030415
AU 2003221968	A1	AU 2003-221968	20030415

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003221968	A1 Based on	WO 2003093806

PRIORITY APPLN. INFO: US 2002-138882 20020503
AN 2004-212650 [20] WPIX
AB US2003207255 A UPAB: 20040324
NOVELTY - A biosensor (I) comprises a substrate, with a receptive layer uniformly covering the substrate, where the receptive material is specific for an analyte of interest and has a pattern of at least one active and inactive areas, the receptive material in the inactive area is rendered

inactive by a blocking agent, and the active and inactive areas are defined by a masking process.

DETAILED DESCRIPTION - A biosensor (I), comprising a substrate (4); a receptive material layer (2) generally uniformly covering a side of the substrate, the receptive material being specific for an analyte of interest (II); a pattern of at least one active area (20) and at least one inactive area (22) of the receptive material defined in the receptive material layer, the receptive material in the inactive area rendered inactive by a blocking agent (6); where a mask (8) having at least one shielded region (10) and at least one exposed region (12) is used to define the active and inactive areas in a masking process; and where when (I) is exposed to a medium containing the analyte of interest, the analyte **binds** to the receptive material in the active areas and facilitates subsequent diffraction of transmitted or reflective light in a diffraction pattern corresponding to the active areas.

An INDEPENDENT CLAIM is also included for making a biosensor, involves forming a receptive material layer generally uniformly over a surface of a substrate, the layer containing a receptive material specific for an analyte of interest; defining at least one active area and at least one inactive area of the receptive material in a masking process, where a blocking agent is used to render the receptive material inactive in the defined inactive area; and where when (I) is exposed to a medium containing the analyte of interest, the analyte **binds** to the receptive material in the active areas and facilitates subsequent diffraction of transmitted light or reflected light in a diffraction pattern corresponding to the active areas.

USE - (I) is useful for detecting (II) such as bacteria, yeast, fungus, virus, rheumatoid factor, IgG, IgM, IgA, IgD and IgE antibodies, carcinoembryonic antigen, Streptococcus Group A antigen, viral antigens, antigens associated with autoimmune disease, allergens, tumor antigens, Streptococcus group B antigen, HIV I or HIV II antigen, antibodies to viruses, antigens specific to Rous sarcoma virus (RSV), an antibody, antigen, enzyme, hormone, polysaccharide, protein, lipid, carbohydrate, drug, nucleic acid, Neisseria meningitidis group A, B, C, Y and W sub 135, Streptococcus pneumoniae, Escherichia coli K1, Haemophilus influenza type A/B, an antigen derived from microorganisms, prostate specific antigen (PSA) and C-reactive protein (CRP) antigens, a hapten, a drug of abuse, a therapeutic drug, an environmental agent, or antigens specific to Hepatitis (claimed). (I) is used in the detection of chemical or biological contamination in garments,such as diapers, the detection of contamination by microorganisms in prepacked foods such as meats, fruit juices or other beverages, and in health diagnostic applications such as diagnostic kits for the detection or protein, hormones, antigens, nucleic acids, microorganisms, and blood constituents. (I) can also be used on contact lenses, eyeglasses, window panes, pharmaceutical vials, solvent containers, water bottles, band-aids, wipes, etc., to detect contamination.

ADVANTAGE - (I) can be mass produced at a low cost, and is disposable. (I) is capable of reliable and sensitive detection of analytes, and avoids possible drawbacks of conventional microcontact printing techniques.

DESCRIPTION OF DRAWING(S) - The figure shows the method for producing biosensors.

receptive material layer 2
substrate 4
blocking agent 6
mask 8
shielded region 10
exposed region 12
active area 20

inactive area 22
Dwg.1/1

L44 ANSWER 22 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-10610 BIOTECHDS
TITLE: Methods for detecting one or more non-nucleic acid analytes using fusion polypeptides with specificity for the analyte, where the polypeptide comprises first and second inactive functional domains and an analyte **binding** domain; enzyme electrode, biosensor, DNA array and high throughput screening, useful for diagnosis
AUTHOR: MINSHULL J; DAVIS S C; WELCH M; RAILLARD S A; VOGEL K; KREBBER C
PATENT ASSIGNEE: MAXYGEN INC
PATENT INFO: WO 2002010750 **7 Feb 2002**
APPLICATION INFO: WO 2000-US24182 31 Jul 2000
PRIORITY INFO: US 2000-244764 **31 Oct 2000**
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-206219 [26]
AN 2002-10610 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Methods for detecting one or more non-nucleic acid analyte (NAA) using fusion polypeptides with specificity for the analyte, where the polypeptide comprises a first inactive functional domain, an analyte **binding** domain and a second inactive functional domain, are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a method (M1) for detecting one or more NAA, comprising: (a) providing at least one fusion polypeptide (P1) with specificity for a NAA, where P1 comprises a first inactive functional domain, an analyte **binding** domain, and a second inactive functional domain, where **binding** of the NAA results in a conformational change which brings the first inactive functional domain and the second inactive functional domain into proximity, therefore converting the first and second inactive functional domains into an optically detectable functional domain; (b) contacting P1 with a sample comprising the NAA; and (c) detecting the conformational change induced by **binding** of the NAA, where the NAA is selected from a small organic molecule, a peptide, a polypeptide and a dissolved gas; (2) another method (M2) for detecting one or more NAA, comprising: (a) step (a) of M1, where the first and second inactive functional domains are converted into a catalytic functional domain; (b) providing a substrate for the catalytic functional domain; (c) contacting the fusion polypeptide with a sample comprising the analyte; and (d) detecting the conversion of the substrate to a product; (3) another method (M3) for detecting one or more NAA, comprising: (a) providing at least one polypeptide with specificity for a NAA, where the polypeptide comprises an analyte **binding** domain and a catalytic domain, where **binding** of the analyte results in an allosteric conformational change which activates the catalytic domain resulting in conversion of a substrate to a detectable product; and (b) providing a substrate for the catalytic domain; (c) contacting the polypeptide with a sample comprising the analyte; and (d) detecting the product produced by activity of the catalytic domain on the substrate; (4) a method (M4) for detecting an analyte, comprising providing at least one biopolymer which undergoes a conformational change upon **binding** to an analyte, contacting a sample comprising the analyte to the biopolymer; and detecting the conformation change induced by **binding** of the analyte, where the analyte is not an ion; (5) a method (M5) for identifying a physiologic state, comprising providing at least one biopolymer which biopolymer undergoes a conformational change

upon **binding** to a marker associated with a physiologic state, contacting the biopolymer with a biological sample comprising the marker, and detecting the conformation change induced by **binding** of the marker, thereby identifying the physiologic state associated with the marker; (6) a biosensor comprising: (a) a support; and (b) at least one polypeptide with specificity for a NAA, where the polypeptide comprises an analyte **binding** domain and a catalytic domain, where **binding** of the analyte results in an allosteric conformational change which activates the catalytic domain resulting in conversion of a substrate to a detectable product, where the polypeptide is **immobilized** on the support; or (c) at least one fusion polypeptide with specificity for a NAA, where the polypeptide comprises a first inactive functional domain, and analyte **binding** domain, and a second inactive functional domain, where **binding** of the analyte brings the first inactive functional domain and the second inactive functional domain into proximity, thereby converting the first and second inactive functional domains into a functional catalytic or optically detectable domain where the fusion polypeptide is **immobilized** on the support; or (d) a polypeptides **immobilized** on the solid support, where the polypeptides having different analyte **binding** specificities, and a detection system; (7) a method (M6) of sensing one or more test stimulus, comprising: (a) providing a library of biopolymers comprising nucleic acid variants or expression products of the nucleic acid variants; (b) arraying the library in a spatial or logical format to provide a physical or logical array; (c) contacting one or more calibrating stimulus to the array, where one or more members of the array produce one or more detectable signals in response to contact by the one or more calibrating stimulus, thereby producing a calibrating array pattern which identifies contact of the array by the one or more calibrating stimulus; (d) contacting at least one test stimulus to the array, thereby producing a test stimulus array pattern; and (e) comparing the test stimulus array pattern to the calibrating array pattern, thereby identifying the test stimulus; (8) a method (M7) of using a re-usable array of biopolymers, comprising: (a) providing a physical or logical array of biopolymers comprising nucleic acid variants or expression products of the nucleic acid variants; (b) contacting the physical or logical array with one or more first stimulus; (c) observing a first resulting response of the array, or collecting a first product resulting from contact between the array and the first stimulus; (d) reusing the array by contacting the array a second time with the first stimulus, or with a second stimulus, and observing a second resulting response of the array, or collecting a second product resulting from contact between the array and the first or second stimulus, and, optionally, comparing the first resulting response of the array to the second resulting response of the array; (9) biopolymer array produced by M6 or M7; and (10) a computer comprising a data set corresponding to the labeling biopolymer sensor array pattern or test biopolymer sensor array pattern of M6 or M7.

BIOTECHNOLOGY - Preferred Method: In M1, the first and second inactive functional domains are derived from a green fluorescent protein or a green fluorescent protein homologue. M1 comprises detecting an electrochemical signal produced by **binding** of the analyte or detecting an optical signal produced by **binding** of the analyte. The optical signal is detected by one or more of: ultraviolet spectrophotometry, visible light spectrophotometry, surface plasmon resonance; calorimetry, fluorescence polarization; fluorescence quenching; colorimetric quenching; fluorescence wavelength shift; fluorescence resonance energy transfer (FRET); enzyme linked immunosorbent assay (ELISA) or liquid crystal displays (LCD). The optical signal is produced by displacement of a tethered substrate upon

binding of the analyte. The tethered substrate is an analyte analogue. In M2, the conversion of the substrate to a product is detected by detecting an electrochemical signal or an optical signal which is detected as described above. M1, M2, M3, M4 and M5 comprise providing a physical or logical array comprising polypeptides which have different analyte **binding** specificities. In M1, M2, M4 and M5, the polypeptides provide a common signal. The NAA comprises a small molecule, a hormone or a metabolite. The sample is a biological sample (blood, plasma, urine, sweat, cerebrospinal fluid and tears) or an environmental sample. In M3, the conversion of the substrate to product produces an electrochemical signal or an optical signal which is detected as described above. In M3, the conversion of substrate to product by the analyte-**bound** polypeptides is detected by detecting a common signal. The sample is a biological sample, an environmental sample, or an industrial sample. The sample further comprises an agonist or an antagonist. The analyte comprises a small molecule, a hormone, a metabolite, an ion, an **antigen** or a ligand. In M4, the biopolymer comprises a polypeptide which comprises an **antibody** or a receptor. The conformation change results in generation of an optical signal which is detected as described above. The optical signal is produced by displacement of a tethered substrate upon **binding** of the analyte. The tethered substrate is an analyte analogue. In M5, the biopolymer comprises a polypeptide which comprises an enzyme, an **antibody**, a receptor or a fusion protein. Preferably the polypeptide is P1, where **binding** of the analyte results in a conformational change which brings the first inactive functional domain and the second inactive functional domain into proximity, thereby converting the first and second inactive functional domains into a functional catalytic or fluorescent domain. The conformation change results in generation of an optical signal which is detected as described above. The optical signal is produced by displacement of a tethered substrate upon **binding** of the analyte. The tethered substrate is an analyte analogue. In M6 and M7, the biopolymer library comprises or is encoded by recursively recombined nucleic acids. The biopolymer library comprises or is encoded by artificially mutated or artificially shuffled nucleic acids. Alternatively, the biopolymer library comprises or is encoded by species variants of one or more nucleic acids. Alternatively, the biopolymer library comprises or is encoded by nucleic acids produced by recursive recombination of species variants of one or more nucleic acids. The biopolymer library comprises photoactivatable members. The method comprises masking a portion of the array and exposing the resulting masked array to light. The array comprises one or more of a conductive member, a capacitive member, an optically responsive member, an electrically responsive member, and an electrically or logically gated or gateable member. Alternatively, the array comprises one or more of: a bio-laser, a polychromic display, a molecular poster, a bar code, a protein TV, a molecular camera, a UV (ultra-violet) molecular camera, an IR (infra-red) molecular camera, or a flat screen display. The array members comprise one or more proteins. The proteins comprise electrically conductive proteins. The proteins are purified. The proteins comprise one or more purification tags such as His tags, and FLAG tags. Arraying the biopolymer library comprises: (a) arranging the members of the library in a logically accessible format; (b) arranging the members of the library in a physically grided format; (c) plating the members of the library in microtiter trays; or (d) arranging the members of the library for parallel examination. Arraying the biopolymer library or expression product library comprises recording the position of members of the library in one or more database, or arranging the members of the library for sequential examination. The first, second, test or calibrating stimulus are simultaneously, sequentially or alone contacted to

biopolymer library members. Contact of the of first, second, test or calibrating stimulus produces a signature for a sample type. The signature is representative of one or more phenomenon selected from a metabolic state of a cell, an operon induction in or by a cell, an induction of cell growth, a proliferation in or caused by a cell, a cancer of a cell or tissue, or organism, apoptosis, cell death, cell cycle, cell or tissue differentiation, tumorigenesis, disease state, drug resistance, drug efficacy, antibiotic spectrum, drug toxicity, gas level, SOx, NOx Alzheimer's disease, infection, presence of viruses, viral infection, bacterial infection, HIV infection, AIDS, serum cholesterol, CHDL (undefined) level, LDL (low density lipoprotein), serum triglyceride level, blood glucose level, ion or gas production or internalization, cytokine receptor expression, **antibody-antigen** interactions, pregnancy, fertility, fecundity, presence or absence of narcotics or other controlled substances, heart attack, presence or absence of steroids, body temperature, presence of sound waves, taste, scent, food composition, beverage composition, and an environmentally monitored condition. The first, second, test or calibrating stimulus are contacted to library members in a microtiter plate or fixed on a solid substrate. Alternatively, the first, second, test or calibrating stimulus are contacted to library members, or their expression products, fixed on a solid substrate, where the solid substrate comprises a Nickel-NTA coated surface, a silane-treated surface, a pegylated surface, or a treated surface. The biopolymer library members or expression products thereof are fixed to an organizational matrix in spatially addressable locations. Alternatively, the first, second, test or calibrating stimulus are contacted to biopolymer library members, where member types are fixed on the surface of one or more beads. One or more beads each comprise more than one detectable feature. More than one detectable feature includes a first feature which identifies **binding** by the first, second, test or calibrating stimulus and a second feature which identifies either the type of bead or the type of library member or expression product thereof which is **bound** to the bead. The first stimulus, the second stimulus, the calibrating stimulus or the test stimulus, is selected from light, radiation, an atom, an ion, and a molecule. The first, second, test or calibrating stimulus comprises, hybridizes to, **binds**, acts upon or is acted upon by one or more of: radiation, a polymer, a chemical group, a biopolymer, a nucleic acid, an RNA, a DNA, a protein, a ligand, an enzyme, a chemo-specific enzyme, a regio-specific enzyme, a stereo-specific enzyme, a nuclease, a restriction enzyme, an restriction enzyme which recognizes a triplet repeat, a restriction enzyme that recognizes DNA superstructure, a restriction enzyme with an 8 base recognition sequence, an enzyme substrate, a regio-specific enzyme substrate, a stereo-specific enzyme substrate, a ligase, a thermostable ligase, a polymerase, a thermostable polymerase, a co-factor, a lipase, a protease, a glycosidase, a toxin, a contaminant, a **metal**, a heavy **metal**, an immunogen, an **antibody**, a disease marker, a cell, a tumor cell, a tissue-type, cerebrospinal fluid, a cytokine, a receptor, a chemical agent, a biological agent, a fragrance, a pheromone, a hormone, an olfactory protein, a metabolite, a molecular camera protein, a rod protein, a cone protein, a light-sensitive protein, a lipid, a pegylated material, an adhesion amplifier, a drug, a potential drug, a lead compound, a protein allele, an oxidase, a reductase, or a catalyst. The first, second, test or calibrating stimulus are contacted to the members of the library by incubating a solution comprising the test molecule or the calibrating molecule with the library members. The solution is a fluid, a polymer solution or a gel. Comparison of the test array pattern and the calibrating array pattern, or of the first resulting response of the array and the second resulting response of the array, is performed by a computer. The first, second, test or calibrating

stimuli are contacted to the array to produce resulting array patterns. The methods further comprise recording the resulting array patterns in one or more databases, and assigning a bar code to each resulting array pattern. The test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array, comprises variations in the presence or absence of signal at different locations on or in the array. The test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array comprises variations in the level of signal at different locations on the array. The test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array comprises variations in the presence and intensity of signal at different locations on the array. An intensity of the test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array comprises is measured to quantify the first, second, test or calibrating stimulus. The test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array comprises one or more fluorophore emission, photon emission, chemiluminescent emission, coupled luminescent/fluorescent emission or quenching, or detection of one or more fluorophore emission. The test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array comprises an electrochemically detectable signal, an amperometrically detectable signal, a potentiometrically detectable signal, a signal detectable as a change in pH, a signal based on specific ion levels, a signal based on changes in conductivity, a pizoelectric signal, a change in resonance frequency, a signal detectable as surface accoustic waves, or a signal detectable by quartz crystal microbalances. The test array pattern, the calibrating array pattern, the first resulting response of the array or the second resulting response of the array comprises multiple wavelengths of light. The test array pattern, the calibrating array pattern, the first resulting response of the array or the second resulting response of the array is generated by detection of one or more of: light, H2O2, glucose oxidase, NADP, NADPH+, NAD(P)H reductase, a change in reduction potential, a change in protein conformation, a change in intrinsic fluorescence, fluorescence, luminescence, FRET, absorption, surface plasmon resonance, **antigen binding**, **antibody binding**, enzyme activity, opening of an ion channel, or label **binding.** At least one member of the biopolymer library, or an expression product thereof, is selected, prior to the arraying step, for one or more of: enhanced stability, orientation of protein **binding**, improved production, cost of manufacture, optimal activity of expressed members which comprise a tag, overexpression mutations, optimized protein folding, permanent enzyme secretion, improved operators, improved ribosome **binding** sites, avidity, selectivity, production of a detectable side product, and detection limit. The test array pattern, the calibrating array pattern, the first resulting response of the array or the second resulting response of the array are detected by one or more of: a microscope, a CCD, a phototube, a photodiode, an LCD (liquid crystal display), a scintillation counter, film, or visual inspection. The test array pattern, the calibrating array pattern, the first resulting response of the array or the second resulting response of the array are digitized and stored in one or more database in one or more computer. M6 and M7 further comprise contacting at least one additional stimulus to the array, and comparing a resulting additional test stimulus array pattern to the calibrating array pattern, thereby identifying the at least one additional stimulus, or observing an additional resulting response of the array, or collecting an additional product resulting from

contact between the array and the additional or a previous stimulus, and optionally comparing the additional resulting response to any one or more previous responses of the array. The method comprises contacting the array with 2, preferably 10, or more additional stimuli. Preferred Biosensor: The biosensor further comprising a conductive element or an optically detectable element. The polypeptides are **immobilized** with an **immobilization** matrix selected from carbon paste and a non-biological polymeric matrix. The biosensor further comprises a display. Preferred Biopolymer Array: The biopolymer array is stable for at least one year under pre-selected storage conditions.

USE - The methods and biosensors are useful for detecting a wide range of biological, chemical and biochemical stimuli, e.g. polypeptides, hormones, metabolite and small molecules. They are useful in medical, environmental and industrial diagnostic procedures, for e.g. the array can be used for detection of protein biomarkers associated with disease or other physiological condition.

EXAMPLE - Regardless of the format of the library array, calibration and standardization is performed by exposing the array components to one or more known standard, e.g., calibrating or pattern forming, stimulus. For example, to standardize and calibrate the array for detection of small organic molecules, the array is contacted with known organic molecules, e.g., phenol, toluene, xylenol, and selected derivatives. The resulting response, e.g., luciferase or GFP (green fluorescent protein) activity, or calibrating array pattern, is detected and recorded, for example, by a CCD camera or other photoelectric device. The array is then exposed to one or more test stimulus. In the case of cultures, this can be accomplished by exposing replicate cultures to one or more test compounds, while in the case of proteins arrayed on a chip, this is best accomplished by washing under conditions amenable to preservation of the array, followed by subsequent exposure to the test compounds. Alternative formats for performing detection assays, e.g., on microfluidic devices (e.g., LabMicrofluidic device (RTM) high throughput screening system (HTS) by Caliper Technologies, Mountain View, CA or the HP/Agilent technologies Bioanalyzer using LabChip (TM) technology by Caliper Technologies Corp. See, also, www.calipertech.com) are available and favorably employed in the context of the present invention.(159 pages)

L44 ANSWER 23 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-06404 BIOTECHDS
TITLE: **Metal** deposition method, useful for nanofabrication, involves reacting enzyme with substrate to form second substrate, reacting another enzyme with second substrate and **metal** ion solution, and reducing ions to **metal** in zero oxidation state;
metal deposition involving use of enzyme, oxidizing agent and reducing agent for remediation
AUTHOR: HAINFELD J F
PATENT ASSIGNEE: HAINFELD J F
PATENT INFO: US 2002142411 **3 Oct 2002**
APPLICATION INFO: US 2001-822131 30 Mar 2001
PRIORITY INFO: US 2001-822131 **30 Mar 2001**; US 2001-822131 30 Mar 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-102521 [09]
AN 2003-06404 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Deposition (M1) of **metal**, comprising reacting a first enzyme (E1) with a first substrate (S1) to form a second substrate (S2), reacting a second enzyme (E2) with S2 and a solution of **metal**

ions, and reducing at least some of the **metal** ions to **metal** in a zero oxidation state, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a **metal** reaction method (M2), which involves providing **metal** particles or a **metal** surface, linking to an enzyme substrate, and reacting with an enzyme; (2) a **metal** ion reaction method (M3), which involves providing a **metal** ion, oxidizing agent and reducing agent, providing an enzyme, reacting the enzyme with the **metal** ions, oxidizing agent and reducing agent, and reducing at least some of the **metal** ions to **metal** in a zero oxidation state; (3) a test kit (K) comprising a unit for enzymatically depositing **metal** in a zero oxidation state, where the enzymatically deposited **metal** provides a detectable test result; (4) a biosensor (BS) for providing a signal related to changes in a selective test condition, comprising an enzyme, an enzyme substrate reactable with the enzyme, where the reaction of the enzyme and enzyme substrate provides a signal proportional to a selective test condition, and a unit for detection of the signal; and (5) a test method (M4), which involves providing a first material comprising one of an enzyme or enzyme substrate, exposing the first material to a test sample, where the first material will attach to a selective target if the test sample includes the target, reacting the test sample with a second material comprising a first unit selected from **metal** ions, **metal** particles or their mixtures, and a second unit comprising the other of the enzyme or enzyme substrate, and enzymatically accumulating **metal** in a zero oxidation state if the target is present in the test sample.

BIOTECHNOLOGY - Preferred Method: M1 further involves exposing a cell to **metal** ions, and enzymatically reducing the **metal** ions to **metal** in a zero oxidation state within the cell. The cell is alive during exposure, and remains alive during enzymatic reduction. M2 involves holding or depositing the **metal** particles near the enzyme, preferably within 1 micron. A number of **metal** particles are provided, and at least some of the **metal** particles are accumulated near the enzyme. At least a partial organic coating is formed on at least some of the **metal** particles and is linked to the enzyme substrate by attaching the enzyme substrate to the organic coating. Alternatively, the substrate is incorporated into the coating. The **metal** particles are at least partially covered with organic coating. The coating is enzymatically altered or chemical group of the coating is enzymatically cleaved on reacting with the substrate. The **metal** particles are each of diameter 0.8-50 nm, and are silver, gold, iron, mercury, nickel, copper, platinum, palladium, cobalt, and/or iridium. The enzyme is oxido-reductase, hydrolase, transferase, phosphorylase, decarboxylase, hydrase, and/or isomerases M2 further involves pre-treating the enzyme with **metal** ions before deposition. In M3, the **metal** ions, oxidizing agent and reducing agent are part of a developing mix, and the reaction involves reacting the enzyme with a developing mix; initially reacting the enzyme with a pretreatment solution of **metal** ions and subsequently reacting the enzyme with the developing mix; or initially reacting the enzyme with a pretreatment solution of **metal** ions selected from gold ions and silver ions, and subsequently reacting the enzyme with the developing mix. The developing mix comprises **metal** ions, oxidizing agent and the reducing agent in a pH buffer. The **metal** ions are silver ions, the oxidizing agent is hydrogen peroxide, the reducing agent is hydroquinone. The method further involves depositing the zero oxidation state **metal** within a cell. The enzyme is localized to an **antigen**, predetermined **antigen**, nucleic acid or nucleic acid probe, **antibody**, **antibody** fragments, peptide,

carbohydrates, drugs, steroids, products from plants, animals, human and bacteria, and synthetic molecules that have an affinity for **binding** particular agents. Coating is autometallographically formed over at least a portion of the **metal.** The **metal** ion acts as a substrate for the enzyme. An object may be made by treating a biological structure with a **binding** moiety, localizing an enzyme to the **binding** moiety, and enzymatically depositing **metal** in the vicinity of the enzyme. A remediation process may be conducted by providing a carrier stream containing **metal** ions, **metal** particles or their mixtures, reacting an enzyme and an enzyme substrate with the carrier stream, and enzymatically depositing the material.

USE - Useful for deposition **metal** in a cell, for fabricating an object, or in remediation (claimed). The method is also useful in highly sensitive gene and protein detection, sensitive immunodetection, novel biosensor designs, for probing in microscopy, bacterial detection and in remediation. The enzymatic **metal** deposits thus formed are useful in immunohistochemistry and immunocytochemistry, in situ hybridization techniques, lateral flow diagnostics, Western, Southern and other blots, and other tests performed on membranes. The deposits are also useful for sensitive detection of **antigens** and other materials.

ADVANTAGE - No harmful radioactivity need be handled or disposed of to achieve comparable or better sensitivity in assays. No lengthy time of exposure is need (autoradiograms can take several months to expose). No film, film processing or film chemicals are required. No expensive fluorescent optics, light sources or filters are required. There is no fading of the sample upon observation or storage or exposure to room lights. Autofluorescence from cells and other molecules does not create any interference. Standard stains (e.g. nuclear fast red, hematoxylin and eosin) can be used and seen simultaneously with the enzyme deposited **metals**, thus enabling visualization of landmarks of a tissue simple. No expensive chemiluminescence equipment or substrate, and/or film development is necessary. The enzyme deposited **metals** create a permanent record. Sensitive detection can be relatively quick. The method can provide more sensitive and rapid detection than is possible with non-enzymatic methods.

EXAMPLE - One micro-g of horseradish peroxidase was applied to a nitrocellulose membrane and allowed to dry. The membrane was then optionally blocked using 4 % bovine serum albumin and washed. A solution containing 2.5 mg/ml hydroquinone and 1 mg/ml silver acetate in a 0.1 M citrate buffer, pH 3.8 was applied. Hydrogen peroxide was added and mixed to a final concentration of 0.03-0.06 %. Silver deposition selectively occurred at the peroxidase spot as evidenced by a black product. No deposit occurred if the hydrogen peroxide was omitted. Human breast cancer biopsies were fixed, embedded and sectioned. In situ hybridization was performed by removal of paraffin, treatment with proteinase K and hybridization with a fluoresceinated probe for Her-2/neu gene. After hybridization and washing, a biotinylated anti-fluorescein **antibody** was applied, followed by streptavidin conjugated to horseradish peroxidase. The sample was then pretreated with a gold salt solution, and after washing, was exposed to silver acetate, hydroquinone and hydrogen peroxide. Silver deposits appeared at the targeted gene site and were evident by bright field light microscopy. This demonstrated the high sensitivity of the enzyme **metal** deposition to detect single gene copies within individual cells. (18 pages)

L44 ANSWER 24 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-10149 BIOTECHDS
TITLE: Depositing transfer material comprising a biomaterial on a

receiving substrate for creating a pattern of biomaterial on the substrate, involves using a source of laser energy, receiving substrate and a target substrate;
DNA, RNA, cell, protein **immobilization** useful for biosensor, bioarray construction and tissue engineering

AUTHOR: RINGEISEN B R; CHRISEY D B; PIQUE A; MCGILL R A
PATENT ASSIGNEE: RINGEISEN B R; CHRISEY D B; PIQUE A; MCGILL R A
PATENT INFO: US 2002122898 **5 Sep 2002**
APPLICATION INFO: US 2002-68315 8 Feb 2002
PRIORITY INFO: US 2002-68315 **8 Feb 2002**; US 1999-117468 27 Jan 1999
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-208932 [20]
AN 2003-10149 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Depositing (M1) a transfer material on a receiving substrate (18) by exposing a target substrate containing a laser-transparent support (15) having a composite material (16), to laser energy (14), which causes desorption of composite material from the support surface and deposits it at a defined receiving location on the substrate.

DETAILED DESCRIPTION - Depositing (M1) a transfer material on a receiving substrate (18) comprises exposing a target substrate having a laser-transparent support (15) with a laser-facing surface and a support surface, the support having a composite material (16) with a back surface in contact with support surface, to laser energy (14), which causes desorption of composite material from the support surface and deposits it at a defined receiving location on substrate. The target substrate comprises a laser-transparent support having a laser-facing surface and a support surface. The target substrate also comprises a composite material having a back surface in contact with the support surface and a front surface facing the substrate. The composite material comprises a mixture of the transfer material to be deposited and a matrix material. The matrix material is a material that has the property that, when it is exposed to laser, it desorbs from the laser-transparent support. The source of laser energy (12) is positioned in relation to the target substrate so that laser energy is directed through the laser-facing surface of the target substrate and through the laser-transparent support to strike the composite material at a defined target location. The receiving substrate is positioned in a spaced relation to the target substrate. The source of laser energy has sufficient energy to desorb the composite material at the defined target location, causing the composite material to desorb from the defined target location and be lifted from the support surface of the laser-transparent support. The composite material is deposited at a defined receiving location on the receiving substrate.

BIOTECHNOLOGY - Preferred Method: The method is controlled by a computer and is carried out under controlled conditions such as humidity, atmospheric composition, air pressure, room temperature and sterility. The source of laser energy is a pulsed laser and is focussed through an objective. The laser energy and receiving substrate are positioned through a laser positioning unit (20), a target substrate positioning unit (22) and a receiving substrate positioning unit (24). Positioning the units and exposing the target substrate are repeated at successive defined target locations and successive defined receiving locations and the composite material is deposited in a two- or three-dimensional pattern of deposited composite material. Initially, the receiving substrate is positioned in a spaced relation to the source of laser energy and exposed to the laser energy so that the laser energy machines

away a defined machining location on the receiving substrate. The composite material is deposited into a defined machining location that has been previously machined away by the laser energy. Different composite materials are deposited in respective patterns on the receiving substrate, by repeating the steps one or more times using target substrates comprising different composite materials, which comprise different transfer materials. One or more composite materials comprises a matrix material and an electronic transfer material, such as **metal**, dielectric, resist and/or semiconductor, and one or more electronic transfer materials are used to create electronic circuitry on the substrate. The laser-transparent support comprises quartz or machine etched quartz, and a laser-transparent flexible polymer ribbon. The support surface of the laser-transparent support comprises a laser-absorbing layer in contact with the back surface of the composite material and the laser absorbing layer is vaporized by the laser energy. The laser absorbing layer comprises gold, chrome and titanium. The receiving substrate comprises chemically functionalized glass, polymer-coated glass, quartz, natural hydrogel, synthetic hydrogel, uncoated glass, nitrocellulose coated glass, silicon, glass, plastics, **metals** and ceramics. The substrate comprises covalent and/or physisorbed functionalization chosen from a living host, (non)living cell, living cell culture, non-living group of cells, living tissue, chemically or biologically functionalized surface. The composite material is about the incubation temperature of the biomaterial, preferably at -50degreesC - 100degreesC and is frozen to the laser-transparent support. The matrix material comprises glycerol, water, polymer, cell medium, cell nutrient, natural or synthetic hydrogel, surfactant, antibiotic, **antibody**, **antigen**, protein, dimethyl sulfoxide, water/dimethylsulfoxide mixture, agarose, saline solution, dielectric particles, **metal** particles, aqueous inorganic salt solution, nitrocellulose gel, sol gel, ceramic composite, DNA, RNA or protein-coated particles. The matrix material preferably comprises a mixture of water and glycerol.

USE - (M1) is useful for depositing a transfer material comprising a biomaterial (living or active) such as proteins, hormones, enzymes, **antibodies**, DNA, portions of DNA strands, inorganic nutrients, aqueous salt solutions, RNA, nucleic acids, aptamers, **antigens**, lipids, oligopeptides, polypeptides, cofactors and polysaccharides on a receiving substrate. The biomaterial remains living or active on the receiving substrate. The biomaterial may also comprise one or more materials such as single cell, groups of cells, living cells, multi-cell assemblies, pluripotent cells, stem cells, heart, lung cells, muscle cell neurons and neural networks, living tissue, skin, hair or nail producing tissue, and brain tissue, DNA/RNA-coated particles or protein-coated particles and one or more functional supporting media such as nutrients and other life supporting material. The biomaterial comprises one or more tagging compounds such as organic and inorganic tagging compounds. The deposited composite material is an engineered cellular or composite structures for growth, repair, replacement or improvement of tissue, a living organ, a device to investigate inter and intracellular signaling, a living device to control or divert the flow of fluid through microfluidic channels, a living miniature electrode, a neural network, a device to investigate cell aging, a bridge to connect a nerve synapse, a biofilm, a drug delivery system or coating, an implantable drug delivery system, a chemical or biological sensing device to sense chemicals or biomaterials, an implantable, biocompatible sensor/signaler device (all claimed).

ADVANTAGE - A pattern of deposited composite material can be created directly on the receiving substrate without the use of a mask. A wide range of transfer materials including living or active biomaterials with

no damage to the transfer materials. Transfer materials are deposited on a receiving substrate in a controlled manner and it is possible to switch rapidly between different transfer material to be deposited on the receiving substrate.

EXAMPLE - Living mouse stem cells were transferred from a room temperature support. The transfer material was living mouse stem cells. The matrix material was with a hydrogel layered below the living cells. This transfer was performed with 193 nm 30 ns laser pulses at an energy density of less than 20 mJ/cm2. Green fluorescence after laser transfer and 3 days of culture indicated liver cells and near 100% viability. (14 pages)

L44 ANSWER 25 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-15535 BIOTECHDS
TITLE: Preparing biomolecular monolayer useful for preparing kits and biosensors for disease diagnosis, by reacting functional dendrimers on **metal** or glass surface with biomolecules e.g. protein, **antigen**, **antibody**, enzyme;
glucose-oxidase **immobilization** on solid support matrix for biosensor and protein chip construction
AUTHOR: KIM H; YOON H; HONG M
PATENT ASSIGNEE: KIM H; YOON H; HONG M
PATENT INFO: US 2002006626 **17 Jan 2002**
APPLICATION INFO: US 2000-795604 15 Jul 2000
PRIORITY INFO: KR 2000-40829 **15 Jul 2000**
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-328314 [36]
AN 2002-15535 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Preparing biomolecular monolayer, comprising reacting **metal** or glass surface with amine-terminated or succinimide-terminated alkanethiol for 1-2 hours to obtain self-assembled monolayer (I) that is reacted with amine-terminated, or N-hydroxysuccinimide-modified, carboxyl-terminated dendrimers (D) to give (D) monolayer (II), and reacting (II) with protein, **antigen**, **antibody**, enzyme receptor or ligand, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) preparing biomolecular monolayer based on strong interaction between avidin and biotin, comprising reacting (I) on **metal** or glass surface with amine-terminated (D) to obtain (II), reacting (II) with biotin to give biotinylated (II), and reacting biotinylated (II) with avidin to give avidin monolayer which is reacted with biotin-modified biomolecules; (2) preparing microarray of biomolecules by reacting **metal** surface or glass surface with a solution of alkane thiol or derivatized silane with amine reactive functionality to obtain (I), reacting (I) with amine-terminated (D) to give micropattern of (D), and reacting the patterned (D) with a biomolecule of protein, **antigen**, **antibody**, enzyme receptor or ligand; and (3) preparing microarray of biomolecules based on strong interaction between avidin and biotin which involves reacting micropattern of (D) with biotin to obtain biotin-modified microarray of (D), reacting the micropatterned, biotin-terminated (D) with avidin to give a microarray of avidin, and reacting the avidin microarray with the biotinylated biomolecule of protein, **antigen**, **antibody**, enzyme, receptor or ligand.

BIOTECHNOLOGY - Preferred Method: In (M1), the **metal** or glass surface is reacted with an alkane thiol preferably cystamine dihydrochloride. (II) on a glass surface is obtained by reacting amine

chain-end (D) on the surface of aldehyde silane-coated slide glass. (D) is any one of G1, G2, G3, G4 and G5 dendrimers containing amine groups, and G1.5, G2.5, G3.5, G4.5 and G5.5 dendrimers containing carboxyl groups modified with N-hydroxysuccinimide. Preferably, a monolayer of biomolecule containing amine groups or sugar chains is prepared by (M1), where the biomolecules containing amine groups are reacted with N-hydroxysuccinimide-modified, carboxyl-terminated (D), and biomolecules containing sugar chains are reacted with (D) containing amine groups after sugar chains are oxidized with periodate to have aldehyde groups.

USE - Preparing biomolecular monolayers, where the biomolecule contains amine groups or sugar chains (claimed). The method is useful for preparing kits and biosensors for disease diagnosis and compound analysis using more recently, integrated high-throughput analyzing system such as development of protein chips.

ADVANTAGE - Homogeneous high density monolayer of biomolecules can be prepared, and consideration of covalent bonding or orientation of proteins is not necessary.

EXAMPLE - Preparation of monolayer using poly(amidoamine) dendrimers was carried out as follows. Silicon wafer with evaporated gold was cleaned with ethanol dipping and a self-assembled monolayer was obtained by immersing the washed base substrate in a solution of 5 mM dithiopropionic acid bis-N-hydroxysuccinimide ester in dimethylsulfoxide (DMSO) for 2 hours. After washing with methanol, the self-assembled monolayer thus obtained was immersed in a solution of 0.022 mM amine-terminated dendrimer in methanol for 1 hour to obtain a dendrimer monolayer. To prepare a glucose oxidase monolayer, periodate-treated glucose oxidase solution was reacted with the dendrimer monolayer prepared above for 30 minutes to 1 hour. To stabilize imine linkage formed in this reaction, reduction was conducted using sodium borohydride compound for 30 minutes, and free aldehyde groups remained on their periphery of **immobilized** enzymes were blocked by treatment with 10 mM ethanolamine for 30 minutes. The characterization of glucose oxidase monolayer on the film prepared above was performed by electrochemical method as follows. The film with **immobilized** glucose oxidase was dipped into a buffer solution containing enzyme substrate and electron-transferring mediators, and then concentration of resulting **immobilized** enzyme was measured by registering resulting bioelectrocatalyzed current by applying voltage of 250 mV. The concentration of **immobilized** glucose oxidase was estimated by kinetic simulation as 1.7x10 to the power -12 mol/square cm. 80 % of **immobilized** enzyme activity was retained after 20 day storage in a buffer solution under room temperature.(9 pages)

L44 ANSWER 26 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-17962 BIOTECHDS
TITLE: Test strip for detecting biochemical components in a sample, comprises a reaction layer formed by coating working- and reference electrodes with a slurry comprising **metal** particles having a size in nanometers; glucose-oxidase enzyme electode for biosensor construction
AUTHOR: SHEN T Y S; CHEN W; LIN H; CHUANG J
PATENT ASSIGNEE: APEX BIOTECHNOLOGY CORP
PATENT INFO: US 6491803 **10 Dec 2002**
APPLICATION INFO: US 2001-859371 18 May 2001
PRIORITY INFO: US 2001-859371 **18 May 2001**; US 2001-859371 18 May 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-478710 [45]
AN 2003-17962 BIOTECHDS

AB DERWENT ABSTRACT:
NOVELTY - A test strip, comprising: (a) an electrically insulating substrate; (b) a conducting film coated on one side of the insulating substrate;(c) a reaction layer formed by coating the working electrode and the reference electrode with a slurry comprising: (i) a fiber; (ii) **metal** particles having a size in nanometers; and (iii) a bioactive substance; and (d) an electrically insulating layer on the substrate, is new.

DETAILED DESCRIPTION - A test strip, comprising: (a) an electrically insulating substrate (2); (b) a conducting film coated on one side of the insulating substrate to form an isolated and disconnected anode and cathode, the anode being disposed on the substrate and formed with, on both ends of the anode, a working electrode (4) and an anode connector respectively, the cathode being disposed on the substrate and being formed with, on both sides of the cathode, a reference electrode (7) and a cathode connector respectively; (c) a reaction layer (9) formed by coating the working electrode and the reference electrode with a slurry, comprising: (i) a fiber; (ii) **metal** particles having a size in nanometers; (iii) a bioactive substance; (iv) potassium ferricyanide as an electrical mediator; (v) a polymer; and (vi) a surfactant; (d) an electrically insulating layer (10) on the substrate and having an opening (11) for receiving the sample on the reaction layer, is new. INDEPENDENT CLAIMS are also included for: (1) producing the test strip, comprising: (a) coating a conducting film on one side of an electric insulating substrate and forming isolated and disconnected anode and cathode; (b) coating an electric insulating film on a part of the conducting film, where one end of an uncovered anode of the conducting film is at least a reference electrode and the other end an anode connector, and one end of an uncovered cathode of the conducting film is at least a working electrode and the other end a cathode connector; and (c) coating a region containing at least the working electrode, with a slurry comprising: (i) a fiber; (ii) **metal** particles having a size in nanometers; and (iii) a bioactive substance, and the reference electrode to form a reaction film to connect the working electrode and the reference electrode individually; and (2) a biosensor comprising the test strip and a detection device.

USE - The test strip is used for detecting biochemical components in a sample.

ADVANTAGE - The test strip has a superior conductivity in the detection of biomolecules. It does not require several drying steps and forms a uniform and flat reaction layer on a surface. It has multiple sampling sites.

EXAMPLE - A test strip was constructed as follows. A conducting film of carbon ink was screen printed on a flat surface of a PC board substrate to form an anode and a cathode which were independently isolated. The substrate was dried at a temperature of 130degreesC. Then, the polymer of ethyleneglycol and terephthalic acid (PET) electric insulating layer in a thickness of 0.27 mm was disposed on the same side of the flat surface with the conducting film to form an anode connector, a cathode connector, a working electrode and a reference electrode by keeping the conducting film partly exposed. A bioactive substance, comprising: (a) glucose oxidase (3%); (b) potassium ferricyanide (20%); (c) methyl cellulose (2%); (d) cellulose (25%); (e) Triton X-100 (t-Octylphenoxypolyethanol) (1%); (f) glutamic acid (1%); (g) **metal** particle having size of nanometer (1%); and (h) phosphate buffer (pH = 6.5) (47%). was then added onto the reaction area. The test strip was dried at a temperature of 50degreesC for 15 minutes. Then, a reticular covering layer (Teterlon, T120-54) was disposed on the reaction film and the electrode test strip of the biosensor was obtained.(13 pages)

L44 ANSWER 27 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-18744 BIOTECHDS
TITLE: Biosensor for measurement of **antibodies**, comprises labeled **antibodies** adsorbed to **immobilized antigen**, which generates signal by **binding** to electrode if displaced by competition from **antibodies** in sample;
for monoclonal **antibody** analysis
PATENT ASSIGNEE: MATSUSHITA DENKI SANGYO KK
PATENT INFO: JP 2002333419 **22 Nov 2002**
APPLICATION INFO: JP 2001-136007 7 May 2001
PRIORITY INFO: JP 2001-136007 **7 May 2001**; JP 2001-136007 7 May 2001
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2003-485820 [46]
AN 2003-18744 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A biosensor for detecting **antibodies** (11) in a sample fluid (12), is new. Label **antibodies** (17) with attached fat soluble ion-conductive label (16) are pre-adsorbed to an **immobilized antigen** (15) and, if displaced by competing **antibodies** in the sample, are adsorbed onto the working electrode (19), causing a conductivity change in lipid film (21), to generate a signal.
USE - The sensor is useful for detecting an **antibody** in a sample.
ADVANTAGE - Specific **antibodies** in the sample are detected sensitively and accurately using a simple method, with an electrical signal as the output.(10 pages)

L44 ANSWER 28 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-02830 BIOTECHDS
TITLE: Immuno electrode sensor has **immobilized antibody** for detecting composite of test **antigen** in sample and **antibody**, and working electrode with lipid thin film whose ionic conductivity varies depending upon composite;
immunosensor characterization useful for electrochemical and immunoassay analysis
PATENT ASSIGNEE: MATSUSHITA DENKI SANGYO KK
PATENT INFO: JP 2002174614 **21 Jun 2002**
APPLICATION INFO: JP 2000-373892 8 Dec 2000
PRIORITY INFO: JP 2000-373892 **8 Dec 2000**; JP 2000-373892 8 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2002-677216 [73]
AN 2003-02830 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - The sensor has a fat-soluble ion conductive substance-labeled **antibody** (32) of known amount, counter electrode and working electrode having a lipid thin film formed on its surface. The labeled **antibody** and **antigen** (31) in sample react to form composite which is removed by an **immobilized antibody** . The thin film absorbs the excess labeled **antibody** in this reaction, and the ionic conductivity of the thin film is then detected.
BIOTECHNOLOGY - Preferred Sensor: The fat-soluble ionic conductive substance is a polymer or oligomer with a hydrophobic group,

encapsulation compound or a fat-soluble chelating agent. The lipid thin film is a monomolecular film or a multi-layer film, and couples with the **metallic** material of an electrode through a sulfur atom. The lipid thin surface has a hydrophobic group, a non-ionic hydrophilic group, cationic or anionic dissociation group, or amphoteric-ion property dissociation group. The **antibody** is a monovalent **antibody**, especially monoclonal **antibody.**

USE - For electrochemical and immuno analysis.

ADVANTAGE - The sensor rapidly detects **antigen** with high sensitivity, accuracy, and simplicity. (11 pages)

L44 ANSWER 29 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-02829 BIOTECHDS
TITLE: Immuno electrode sensor has working electrode with lipid thin film formed on its surface, and variation of electrical conductivity of thin film detects **antigen**; immunosensor characterization useful for electrochemical and immunoassay analysis
PATENT ASSIGNEE: MATSUSHITA DENKI SANGYO KK
PATENT INFO: JP 2002174613 **21 Jun 2002**
APPLICATION INFO: JP 2000-373890 8 Dec 2000
PRIORITY INFO: JP 2000-373890 **8 Dec 2000**; JP 2000-373890 8 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2002-677215 [73]
AN 2003-02829 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - The sensor has **immobilized antigen** and a fat-soluble ion conductive substance-labeled **antibody** coupled to the **immobilized antigen.** The sensor comprises a working electrode having a lipid thin film formed on its surface, and a counter electrode, where the film absorbs the composite of labeled **antibody** and **antigen** present in the sample. The ionic conductivity of the thin film is then detected.

DETAILED DESCRIPTION - The immunity electrode sensor has a **immobilized antigen**, an **antibody** labeled by the fat-soluble ionic conductive substance and coupled to the **immobilized antigen** by **antigen** **antibody** reaction. A pair of electrodes, a working electrode (51) having a lipid thin film formed on it, and counter electrode are present in the sensor, where the lipid thin film formed on the electrode surface absorbs the composite that is formed when the labeled **antibody** forms complex with the **antigen** present in the sample. The fat-soluble ionic conductive label with a variation of the electrical conductivity of a lipid thin film is detected.

BIOTECHNOLOGY - Preferred Sensor: The fat-soluble ionic conductive substance is a polymer or oligomer with a hydrophobic group, encapsulation compound or a fat-soluble chelating agent. The lipid thin film is a monomolecular film or a multi-layer film, and couples with the **metallic** material of an electrode through a sulfur atom (53). The lipid thin surface has a hydrophobic group, a non-ionic hydrophilic group, cationic or anionic dissociation group, or amphoteric-ion property dissociation group. The **antibody** is a monovalent **antibody**, especially monoclonal **antibody.** The sensor also comprises a buffer.

USE - For electrochemical and immuno analysis.

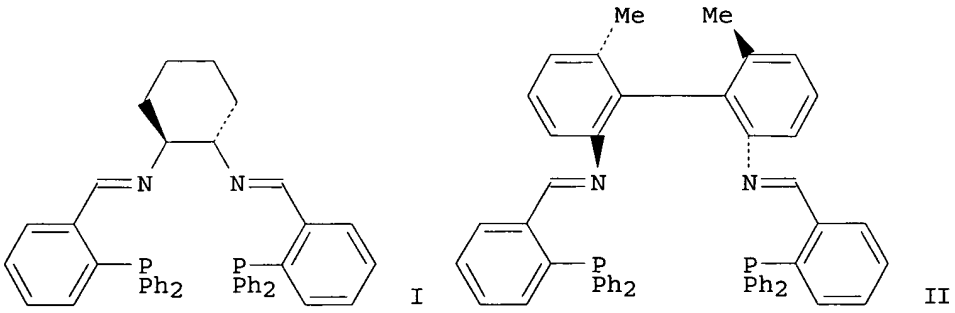
ADVANTAGE - The sensor rapidly detects **antigens** with high sensitivity, accuracy, and simplicity. (10 pages)

L44 ANSWER 30 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:123042 HCAPLUS
DOCUMENT NUMBER: 136:180121
TITLE: Pseudo-**metalloproteins**, their preparation and use in **biosensors**
INVENTOR(S): Lombardi, Angelina; Pavone, Vincenzo
PATENT ASSIGNEE(S): Universita' Degli Studi di Napoli "Federico II", Italy
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012278	A2	20020214	WO 2001-IB1427	20010809 <--
WO 2002012278	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 1317895	B1	20030715	IT 2000-RM454	20000810 <--
AU 2001076606	A5	20020218	AU 2001-76606	20010809 <--
EP 1309612	A2	20030514	EP 2001-954265	20010809 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: IT 2000-RM454 A 20000810 <--
WO 2001-IB1427 W 20010809 <--

OTHER SOURCE(S): MARPAT 136:180121
GI



AB Described herein are Pseudo-**metalloproteins** (M = **metal selected** among Fe, Mn, Ti, Mo, Co, Ni, Cu, Pd, Pt, Au, Ru, Cr, V, Tb, Yb, Rh, Ir, Os; X1 = antigen, or else a functional group that enables association to a biomol.; X2 = functional group that enables association to an **electrode**; S1 and S2 = spacer groups made up of a chain of 3-12 atoms of C, N, O, S and corresponding mixts.; all the other substituents have an amino acid nature), their preparation, and **electrochem. biosensors** containing them. The **biosensors** can be used in

various assays such as diagnostic assays, immunodiagnostic assays, determination of pollutants in water, etc. A peptide-**metal** complex, containing Fe3+ as M; substance P sequence as X1; Cys as X2 and C1-4; Gly-Gly as S1 and S2, was prepared The peptides were synthesized on an automatic peptide synthesizer and then complexed with Fe(SO4)2(NH4)2.

IC ICM C07K014-00

CC 9-1 (Biochemical Methods)
Section cross-reference(s): 15, 29, 34, 61

ST pseudo **metalloprotein biosensor**; peptide **metal** complex **electrochem biosensor**; substance P peptide iron complex

IT Receptors
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(agonists or antagonists, **conjugates** with peptide-based **metal** complexes; pseudo-**metalloproteins**, preparation and use in **biosensors**)

IT Body fluid
Water pollution
(anal. of; pseudo-**metalloproteins**, preparation and use in **biosensors**)

IT Peptides, preparation
RL: ARG (Analytical reagent use); DEV (Device component use); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(complexes, with **metal** ions; pseudo-**metalloproteins**, preparation and use in **biosensors**)

IT **Antigens**
Oligonucleotides
Peptide nucleic acids
Thiols (organic), preparation
RL: ARG (Analytical reagent use); DEV (Device component use); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**conjugates** with peptide-based **metal** complexes; pseudo-**metalloproteins**, preparation and use in **biosensors**)

IT Food preservatives
(determination in foodstuffs of; pseudo-**metalloproteins**, preparation and use in **biosensors**)

IT Toxins
RL: ANT (Analyte); ANST (Analytical study)
(determination of; pseudo-**metalloproteins**, preparation and use in **biosensors**)

IT **Biosensors**
(**electrochem.**; pseudo-**metalloproteins**, preparation and use in **biosensors**)

IT Functional groups
(enabling association with biomol. or with **electrode**; pseudo-**metalloproteins**, preparation and use in **biosensors**)

IT Diagnosis
(immunodiagnosis; pseudo-**metalloproteins**, preparation and use in **biosensors**)

IT Enzymes, preparation
RL: ARG (Analytical reagent use); DEV (Device component use); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(inhibitors, **conjugates** with peptide-based **metal** complexes; pseudo-**metalloproteins**, preparation and use in

biosensors)
IT Polymers, uses
RL: NUU (Other use, unclassified); USES (Uses)
(insol. substrate, in peptide-based **metal** complexes preparation; pseudo-**metalloproteins**, preparation and use in **biosensors**
)
IT Proteins
RL: ARG (Analytical reagent use); DEV (Device component use); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**metalloproteins**, pseudo-; pseudo-**metalloproteins**, preparation and use in **biosensors**)
IT Metabolic pathways
(of drugs, determination of; pseudo-**metalloproteins**, preparation and use in **biosensors**)
IT **Biosensors**
Electrodes
(potentiometric; pseudo-**metalloproteins**, preparation and use in **biosensors**)
IT Amino group
Biochemical molecules
Biosensors
Diagnosis
Drug metabolism
Electrodes
Food analysis
Hydroxyl group
Immobilization, molecular or cellular
Pharmaceutical analysis
Sulfhydryl group
(pseudo-**metalloproteins**, preparation and use in **biosensors**
)
IT Antibodies and **Immunoglobulins**
Antigens
Enzymes, analysis
Nucleic acids
Peptides, analysis
Proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(pseudo-**metalloproteins**, preparation and use in **biosensors**
)
IT Peptides, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(resin-**bound**, in peptide-based **metal** complexes preparation; pseudo-**metalloproteins**, preparation and use in **biosensors**)
IT **Electrodes**
(**voltammetric**; pseudo-**metalloproteins**, preparation and use in **biosensors**)
IT 33507-63-0, Substance P
RL: PRP (Properties)
(peptide-based **metal** complex containing; pseudo-**metalloproteins**, preparation and use in **biosensors**)
IT 58-85-5DP, Biotin, **conjugates** with peptide-based **metal** complexes 7439-88-5DP, Iridium, peptide-based complexes 7439-89-6DP, Iron, peptide-based complexes 7439-96-5DP, Manganese, peptide-based complexes 7439-98-7DP, Molybdenum, peptide-based complexes 7440-02-0DP, Nickel, peptide-based complexes 7440-04-2DP, Osmium,

peptide-based complexes 7440-05-3DP, Palladium, peptide-based complexes 7440-06-4DP, Platinum, peptide-based complexes 7440-16-6DP, Rhodium, peptide-based complexes 7440-18-8DP, Ruthenium, peptide-based complexes 7440-27-9DP, Terbium, peptide-based complexes 7440-32-6DP, Titanium, peptide-based complexes 7440-47-3DP, Chromium, peptide-based complexes 7440-48-4DP, Cobalt, peptide-based complexes 7440-50-8DP, Copper, peptide-based complexes 7440-57-5DP, Gold, peptide-based complexes 7440-62-2DP, Vanadium, peptide-based complexes 7440-64-4DP, Ytterbium, peptide-based complexes
RL: ARG (Analytical reagent use); DEV (Device component use); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(pseudo-**metalloproteins**, preparation and use in **biosensors**
)

IT 396719-12-3P 396719-13-4P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pseudo-**metalloproteins**, preparation and use in **biosensors**
)

IT 7439-89-6DP, Iron, complexes with peptides 396719-12-3DP, complexes with iron and peptides 396719-13-4DP, complexes with iron and peptides
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(pseudo-**metalloproteins**, preparation and use in **biosensors**
)

IT 10045-89-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(pseudo-**metalloproteins**, preparation and use in **biosensors**
)

IT 398141-84-9 398141-85-0
RL: PRP (Properties)
(unclaimed sequence; pseudo-**metalloproteins**, their preparation and use in **biosensors**)

L44 ANSWER 31 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2001-14067 BIOTECHDS
TITLE: Co-**immobilization** of two or more biochemical species on a carrier for detection in biotechnology; **antibody**, DNA or enzyme **immobilization**, silicon, glass, sol-gel or noble **metal** solid support matrix and enzyme electrode for biosensor or DNA biosensor and diagnosis
AUTHOR: Bier F; Ehrentreich-Foerster E
PATENT ASSIGNEE: Bier F; Ehrentreich-Foerster E
LOCATION: Potsdam, Germany; Dresden, Germany.
PATENT INFO: DE 10002895 **19 Jul 2001**
APPLICATION INFO: DE 2000-1002895 17 Jan 2000
PRIORITY INFO: DE 2000-1002895 **17 Jan 2000**
DOCUMENT TYPE: Patent
LANGUAGE: German
OTHER SOURCE: WPI: 2001-433629 [47]
AN 2001-14067 BIOTECHDS
AB Defined co-**immobilization** of two or more biochemical species (A) on a carrier in which each surface is passivated and non-specific adsorption is completely suppressed is claimed. The method is used for defined co-**immobilization** of two or more biochemical species on a carrier. The (A)-coated surface is used for purification (affinity chromatography) and detection of biotechnology, biological analysis, medicine, clinical chemistry and diagnosis, also as a biosensor, e.g. for performing immunoassays. (A) are lipophilic compounds, enzymes (or their complexes, substrates or inhibitors), haptens, hormones, antagonist,

agonist, **antibodies** (or their fragments), **antigens**, lipids, DNA, peptide nucleic acids (or their derivatives), polysaccharides, lipids, markers or labels (e.g. fluorochromes) or mixtures of these. The carrier is a silicon wafer, glass surface, sol-gel material or noble **metal.** Particularly, the surface may form a biosensor, e.g. any sort of electrode, optical sensor, light conductor or coated wave guide. (5pp)

L44 ANSWER 32 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:798541 HCAPLUS
DOCUMENT NUMBER: 135:328923
TITLE: Use of ink-jet printing to produce diffraction-based **biosensors**
INVENTOR(S): Kaylor, Rosann M.; Chidebelu-Eze, Chibueze Obinna; Choi, Abraham B.
PATENT ASSIGNEE(S): Kimberly-Clark Worldwide, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081921	A2	20011101	WO 2001-US11705	20010411 <--
WO 2001081921	A3	20020627		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1277056	A2	20030122	EP 2001-924915	20010411 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-557453 A 20000424 <--
WO 2001-US11705 W 20010411 <--

AB The present invention provides an inexpensive and sensitive device and method for detecting and quantifying analytes present in a medium. The device comprises a **metalized** film upon which is ink-jet printed a specific, predetd. pattern of **binder**, such as an antibody. Upon attachment of a target analyte to **select** areas of the plastic film upon which the **binder** is printed, diffraction of transmitted and/or reflected light occurs via the phys. dimensions and defined, precise placement of the analyte. A diffraction image is produced which can be easily seen with the eye or, optionally, with a sensing device. Gold-coated Mylar was printed at 720 dpi with a thiolated polyclonal antibody to Strep B.

IC ICM G01N033-53
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 10, 15
ST ink jet printing diffraction **biosensor**; antibody printing gold coated Mylar diffraction **biosensor**
IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(E; use of ink-jet printing to produce diffraction-based

biosensors)
IT Aspergillus fumigatus
(allergens **conjugates** with microparticles; use of ink-jet printing to produce diffraction-based **biosensors**)
IT Surfactants
(anionic, in **binder** layer inactivation in pattern; use of ink-jet printing to produce diffraction-based **biosensors**)
IT Proteins, specific or class
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(antibody-**binding**; use of ink-jet printing to produce diffraction-based **biosensors**)
IT Microparticles
(**conjugates** with Aspergillus fumigatus allergens; use of ink-jet printing to produce diffraction-based **biosensors**)
IT **Allergens**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**conjugates** with microparticles; use of ink-jet printing to produce diffraction-based **biosensors**)
IT **Metals**, uses
Polymers, uses
RL: DEV (Device component use); USES (Uses)
(films; use of ink-jet printing to produce diffraction-based **biosensors**)
IT Polyesters, uses
RL: DEV (Device component use); USES (Uses)
(gold-coated; use of ink-jet printing to produce diffraction-based **biosensors**)
IT Optical sensors
(immunol. **biosensors**; use of ink-jet printing to produce diffraction-based **biosensors**)
IT **Biosensors**
(immunol., optical; use of ink-jet printing to produce diffraction-based **biosensors**)
IT **Biosensors**
(immunosensors; use of ink-jet printing to produce diffraction-based **biosensors**)
IT Films
(**metalized**; use of ink-jet printing to produce diffraction-based **biosensors**)
IT Antibodies
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(monoclonal, thiolated, to IgE, printing on gold-coated Mylar film; use of ink-jet printing to produce diffraction-based **biosensors**)
IT **Biosensors**
(optical; use of ink-jet printing to produce diffraction-based **biosensors**)
IT **Biosensors**
Ink-jet printing
Optical diffraction
Plastic films
Streptococcus group B
(use of ink-jet printing to produce diffraction-based **biosensors**)
IT Antibodies
RL: ARG (Analytical reagent use); DEV (Device component use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(use of ink-jet printing to produce diffraction-based

biosensors)
IT 7440-57-5, Gold, uses
RL: DEV (Device component use); USES (Uses)
(Mylar coated with; use of ink-jet printing to produce diffraction-based **biosensors**)
IT 25038-59-9, Mylar, uses
RL: DEV (Device component use); USES (Uses)
(gold-coated; use of ink-jet printing to produce diffraction-based **biosensors**)
IT 151-21-3, Sodium dodecyl sulfate, uses 9001-92-7, Protease
RL: NUU (Other use, unclassified); USES (Uses)
(in **binder** layer inactivation in pattern; use of ink-jet printing to produce diffraction-based **biosensors**)
IT 56-81-5, Glycerin, uses
RL: NUU (Other use, unclassified); USES (Uses)
(monoclonal antibody printing in relation to; use of ink-jet printing to produce diffraction-based **biosensors**)
IT 9003-39-8, Polyvinylpyrrolidone
RL: DEV (Device component use); USES (Uses)
(use of ink-jet printing to produce diffraction-based **biosensors**)
IT 9004-70-0, Nitrocellulose
RL: NUU (Other use, unclassified); USES (Uses)
(use of ink-jet printing to produce diffraction-based **biosensors**)
IT 169751-10-4, Sulfo-LC-SPDP
RL: RCT (Reactant); RACT (Reactant or reagent)
(use of ink-jet printing to produce diffraction-based **biosensors**)

L44 ANSWER 33 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:453361 HCAPLUS
DOCUMENT NUMBER: 135:43091
TITLE: Use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**
INVENTOR(S): Kaylor, Rosann M.; Choi, Abraham B.; Grunze, Michael Heinrich Herbert; Chidebelu-Eze, Chibueze Obinna
PATENT ASSIGNEE(S): Kimberly-Clark Worldwide, Inc., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001044813	A2	20010621	WO 2000-US42768	20001212 <--
WO 2001044813	A3	20020502		
WO 2001044813	C2	20020815		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6399295	B1	20020604	US 1999-465921	19991217 <--

EP 1238277 A2 20020911 EP 2000-992910 20001212 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 1999-465921 A 19991217 <--
WO 2000-US42768 W 20001212 <--

AB The present invention provides an inexpensive and sensitive system and method for detecting analytes present in a medium. The system comprises a diffraction enhancing element, such as functionalized microspheres, which are modified such that they are capable of **binding** with a target analyte. Addnl., the system comprises a polymer film, which may include a **metal** coating, upon which is printed a specific, predetd. pattern of analyte-specific receptors. Finally, the system includes a wicking agent which permits the system to be a single step system which avoids the necessity of any addnl. rinsing steps. Upon attachment of a target analyte to **select** areas of the polymer film, either directly or with the diffraction enhancing element, diffraction of transmitted and/or reflected light occurs via the phys. dimensions and defined, precise placement of the analyte. A diffraction image, such as a hologram, is produced which can be easily seen with the eye or optionally, with a sensing device. A nitrocellulose disk having a hole in the center was placed on top of the sample on **biosensors** for Group B Strep or for IgE to wick away **unbound** particles and excess liquid A diffraction image is visualized when analyte is present using a point light source aimed through the hole.

IC ICM G01N033-53
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 10, 15
ST wicking agent optical diffraction **biosensor**; Streptococcus B detection optical diffraction **biosensor**; IgE detection optical diffraction **biosensor**; nitrocellulose membrane wicking optical diffraction **biosensor**

IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(A, IgA; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(E, IgE; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(G, IgG; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Escherichia coli
(K1; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(M, IgM; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Rous sarcoma virus
(RSV, antigen of; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Autoimmune disease
Human immunodeficiency virus 1
Human immunodeficiency virus 2
Microorganism
Streptococcus group A
Streptococcus group B
(antigen of; use of wicking agent to eliminate wash steps for optical

diffraction-based **biosensors**)

IT Hepatitis
(antigen specific to; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Polysulfones, uses
RL: DEV (Device component use); USES (Uses)
(aromatic; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Surfactants
(as blocking agent; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Albumins, analysis
Polyoxyalkylenes, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as blocking agent; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Latex
(as diffraction enhancing element; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Glass, analysis
Plastics, analysis
Polycarbonates, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as diffraction enhancing element; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Flagella
Pilus
(bacterial; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Flow
(capillary, wicking agents; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Microparticles
(**conjugates** with ALK; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Polyoxyalkylenes, uses
RL: DEV (Device component use); USES (Uses)
(**conjugates** with polyamides; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Polyamides, uses
RL: DEV (Device component use); USES (Uses)
(**conjugates** with polyethylene glycol; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Polymers, uses
RL: DEV (Device component use); USES (Uses)
(films; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Receptors
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(for analyte, printed on **biosensor** in predetd. pattern; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Microspheres
(functionalized; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group A; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT Neisseria meningitidis
(group B; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT Neisseria meningitidis
(group C; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT Neisseria meningitidis
(group W-135; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT Neisseria meningitidis
(group Y; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT Coating materials
(**metal**; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT Glass fibers, uses
RL: DEV (Device component use); USES (Uses)
(microfibers; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT Antibodies
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(monoclonal, thiolated, **immobilized**; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT **Biosensors**
(optical diffraction; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT Films
(polymer; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT **Antigens**
RL: ANT (Analyte); ANST (Analytical study)
(tumor-associated; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT Haemophilus influenzae
(type b; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT Bacteria (Eubacteria)
Blood analysis
Cellophane
Chelating agents
Drugs of abuse
Environmental analysis
Fungi
Membranes, nonbiological
Optical diffraction
Pharmaceutical analysis
Streptococcus pneumoniae
Virus
Yeast
(use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)
IT **Allergens**
Carcinoembryonic antigen
Haptens
Rheumatoid factors

RL: ANT (Analyte); ANST (Analytical study)
(use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Antibodies
Antigens
Carbohydrates, analysis
Enzymes, analysis
Hormones, animal, analysis
Lipids, analysis
Nucleic acids
Polysaccharides, analysis
Proteins, general, analysis
RL: ANT (Analyte); ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT **Metals**, analysis
RL: ARG (Analytical reagent use); ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Oligonucleotides
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Ionomers
Polyamides, uses
Polyesters, uses
RL: DEV (Device component use); USES (Uses)
(use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT Caseins, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(β-, as blocking agent; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT 9002-89-5, Polyvinyl alcohol 25322-68-3, Polyethylene glycol
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as blocking agent; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT 9003-53-6, Polystyrene 9004-34-6, Cellulose, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as diffraction enhancing element; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT 9004-70-0, Nitrocellulose
RL: DEV (Device component use); USES (Uses)
(membrane; use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT 9002-67-9, LH
RL: ANT (Analyte); ANST (Analytical study)
(use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT 7429-90-5, Aluminum, analysis 7439-89-6, Iron, analysis 7440-02-0, Nickel, analysis 7440-06-4, Platinum, analysis 7440-22-4, Silver, analysis 7440-47-3, Chromium, analysis 7440-50-8, Copper, analysis 7440-57-5, Gold, analysis 7440-67-7, Zirconium, analysis 11118-57-3, Chromium oxide 39403-39-9, Gold oxide

RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

IT 9002-88-4, Polyethylene 9003-07-0, Polypropylene 9003-56-9, Acrylonitrile-butadiene-styrene copolymer 9004-34-6D, Cellulose, polymers, uses 9004-35-7, Cellulose acetate 9004-36-8, Cellulose acetate butyrate 9004-48-2, Cellulose propionate 9004-57-3, Ethyl cellulose 9012-09-3, Cellulose triacetate 9016-80-2, Methylpentene polymer 9051-64-3 9057-77-6 24968-79-4, Acrylonitrile-methyl acrylate copolymer 24981-14-4, Polyvinyl fluoride 25038-59-9, Mylar, uses 25322-68-3D, Polyethylene glycol, **conjugates** with polyamides
RL: DEV (Device component use); USES (Uses)
(use of wicking agent to eliminate wash steps for optical diffraction-based **biosensors**)

L44 ANSWER 34 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:208507 HCAPLUS
DOCUMENT NUMBER: 134:234000
TITLE: Spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments
INVENTOR(S): Cremer, Paul S.; Simanek, Eric E.; Yang, Tinglu
PATENT ASSIGNEE(S): The Texas A & M University System, USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001020330	A1	20010322	WO 2000-US25627	20000918 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1218745	A1	20020703	EP 2000-963609	20000918 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.:
US 1999-154576P P 19990917 <--
US 2000-564708 A 20000504 <--
WO 2000-US25627 W 20000918 <--

AB Disclosed are spatially-addressed arrays of discreet fluid lipid bilayers prepared by flexible patterning methods that facilitate the compartmentalization of lipid membranes and aqueous solns. disposed thereon into discreet, spatially-addressable, microarray partitions, onto specific and discreet locations of a substantially planar solid support. This process can either be used in parallel or sequentially to pattern thousands of distinct membranes on a single "biochip", and to assay pluralities of **selected** analyte components contacted with the discreet lipid bilayer compartments for one or more target mols. Also provided are biochip microarray systems and methods for their production that

comprise arrays of confined aqueous compartments disposed upon such compartmentalized lipid bilayers. The aqueous compartments are independently addressable, thereby facilitating reagent delivery, reagent extraction, anal. probe and high-throughput analyte screening methods.

IC ICM G01N033-543
ICS B01J019-00

CC 9-1 (Biochemical Methods)

IT **Histocompatibility antigens**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(MHC (major histocompatibility complex), as nonlipid components in lipid bilayer; spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

IT Glass, uses
Metals, uses
Plastics, uses
Polymers, uses
RL: DEV (Device component use); USES (Uses)
(as inert material for replicator pin; spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

IT **Biosensors**
(compartmentalized lipid arrays; spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

IT Antibodies
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**conjugates**, with Alexa Fluor 594; spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

IT Lipids, biological studies
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(**conjugates**, with dinitrophenyl, in bilayers; spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

IT **Immunoglobulins**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(fragments, as nonlipid components in lipid bilayer; spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

IT **Biosensors**
(immunosensors; spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

IT Proteins, specific or class
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(nucleic acid-**binding**, as nonlipid components in lipid bilayer; spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

IT **Antigens**
Carbohydrates, biological studies
Cardiolipins

Cell adhesion molecules
Ceramides
Cerebrosides
Gangliosides
Glycolipids
Growth factors, animal
Hormones, animal, biological studies
Lipids, biological studies
Lysophospholipids
Neurotransmitters
Nucleic acids
Phosphatidylcholines, biological studies
Phospholipids, biological studies
Polysaccharides, biological studies
Sphingolipids
Sterols
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

IT 330626-83-0DP, Alexa Fluor 594 phalloidin, **conjugates** with antibody
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

IT 9013-20-1D, Streptavidin, **conjugates** with Texas Red
82354-19-6D, Texas Red, **conjugates** with streptavidin
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(spatially-addressed lipid bilayer arrays and lipid bilayers with addressable confined aqueous compartments)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 35 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2001-00484 BIOTECHDS
TITLE: A functional inorganic particle for a microorganism sensor, etc.;
support for bacterium **immobilization** for biosensor construction
PATENT ASSIGNEE: Kanai-Shingijutsu-Kenkyusho
LOCATION: Japan.
PATENT INFO: JP 2000239110 **5 Sep 2000**
APPLICATION INFO: JP 1999-40895 19 Feb 1999
PRIORITY INFO: JP 1999-40895 **19 Feb 1999**
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 2000-597512 [58]
AN 2001-00484 BIOTECHDS
AB A functional inorganic particle for a microorganism biosensor is claimed. The inorganic particle has an organic group containing pyridinium base on its surface. The surface of the inorganic particle is further **bound** to a substance having selective **binding** properties (preferably an **antibody** or **antigen**). The functional inorganic particle is useful for a microorganism aggregating

agent, an antibacterial agent, a microorganism sensor, plant viral disease controlling agent, a composition for an oral cavity, a composition for diagnosis and a carrier for a bioreactor. The inorganic particle is selected from **metals**, **metal** oxides, **metal** nitrides, **metal** carbides, and **metal** sulfides. The organic group is a polymer. The inorganic particle has a diameter of up to 1 um and has a polyvinyl pyridine derivative on the surface. The inorganic particle has a large specific surface area and is useful as a support for bacteria. (7pp)

L44 ANSWER 36 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:421409 HCAPLUS
DOCUMENT NUMBER: 133:40210
TITLE: Patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**
INVENTOR(S): McGrath, Kevin; Kaylor, Rosann M.; Everhart, Dennis S.
PATENT ASSIGNEE(S): Kimberly-Clark Worldwide, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000036416	A1	20000622	WO 1999-US27727	19991122 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001055754	A1	20011227	US 1998-213713	19981217 <--
US 6579673	B2	20030617		
EP 1141709	A1	20011010	EP 1999-960563	19991122 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 762900	B2	20030710	AU 2000-17431	19991122 <--
PRIORITY APPLN. INFO.:			US 1998-213713 A	19981217 <--
			WO 1999-US27727 W	19991122 <--

AB The present invention provides an inexpensive and sensitive device and method for detecting and quantifying analytes present in a medium. The device comprises a **metalized** film upon which is printed a specific, predetd. pattern of an antibody-**binding** protein. Upon attachment of a target analyte to **select** areas of the plastic film upon which the protein is printed, diffraction of transmitted and/or reflected light occurs via the phys. dimensions and defined, precise placement of the analyte. A diffraction image is produced which can be easily seen with the eye or, optionally, with a sensing device. An immunosensor for LH had **immobilized** protein A printed on a gold/Mylar film. The sensor was reacted with monoclonal antibody to LH β.

IC ICM G01N033-543
ICS G01N021-47
CC 9-1 (Biochemical Methods)

Section cross-reference(s): 2, 15
ST patterned deposition antibody protein optical diffraction **biosensor**; LH immunosensor **immobilized** protein A
IT Proteins, specific or class
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(A, as antibody-**binding** protein; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(A; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(E; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT Proteins, specific or class
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(G, as antibody-**binding** protein; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(G; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT Proteins, specific or class
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(L, as antibody-**binding** protein; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(M; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT Proteins, specific or class
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(antibody-**binding**; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT Autoimmune disease
Hepatitis
Human immunodeficiency virus 1
Human immunodeficiency virus 2
Microorganism
Rous sarcoma virus
Streptococcus group A
Streptococcus group B
(antigen of; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT Polysulfones, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(aromatic; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT Albumins, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST

(Analytical study); USES (Uses)
(as blocking material; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**conjugates**; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Polyamides, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(ethylene copolymer; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group A; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group B; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group C; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group W-135; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group Y; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Antibodies
RL: ARG (Analytical reagent use); DEV (Device component use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(**immobilized**; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Optical sensors
(immunol. **biosensors**, for LH; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT **Biosensors**
(immunol., optical, for LH; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT **Biosensors**
(immunosensors, optical, for LH; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(monoclonal, **conjugates**, with polystyrene particles; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Bacteria (Eubacteria)
Biosensors
Candida
Cellophane
Drugs
Drugs of abuse
Environmental analysis
Escherichia coli
Films

Fungi
Microspheres
Optical diffraction
Salmonella
Streptococcus pneumoniae
Virus
Yeast
(patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT **Allergens**
Antibodies
Carbohydrates, analysis
Carcinoembryonic antigen
Enzymes, analysis
Haptens
Hormones, animal, analysis
Lipids, analysis
Nucleic acids
Polysaccharides, analysis
Proteins, general, analysis
Rheumatoid factors
RL: ANT (Analyte); ANST (Analytical study)
(patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT **Antigens**
RL: ANT (Analyte); ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Ionomers
Metals, analysis
Oxides (inorganic), analysis
Polyesters, analysis
Polymers, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Albumins, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(serum, as blocking material; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT **Antigens**
RL: ANT (Analyte); ANST (Analytical study)
(tumor-associated; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Haemophilus influenzae
(type b; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT Caseins, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(β-, as blocking material; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)

IT 9003-53-6DP, Polystyrene, **conjugates** with monoclonal antibody
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(particles; patterned deposition of antibody-**binding** proteins

for optical diffraction-based **biosensors**)
IT 9002-67-9, Luteinizing hormone
RL: ANT (Analyte); ANST (Analytical study)
(patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT 9003-99-0D, Peroxidase, **conjugates** with anti-mouse antibody
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT 7429-90-5, Aluminum, analysis 7439-89-6, Iron, analysis 7440-02-0, Nickel, analysis 7440-06-4, Platinum, analysis 7440-22-4, Silver, analysis 7440-47-3, Chromium, analysis 7440-50-8, Copper, analysis 7440-57-5, Gold, analysis 7440-67-7, Zirconium, analysis 9002-88-4, Polyethylene 9003-07-0, Polypropylene 9003-56-9, Acrylonitrile-butadiene-styrene copolymer 9004-34-6D, Cellulose, compds., analysis 9004-35-7, Cellulose acetate 9004-36-8, Cellulose acetate butyrate 9004-48-2, Cellulose propionate 9004-57-3, Ethyl cellulose 9004-70-0, Nitrocellulose 9012-09-3, Cellulose triacetate 9016-80-2, Methyl pentene polymer 24937-78-8 24968-79-4, Acrylonitrile-methyl acrylate copolymer 24981-14-4, Polyvinyl fluoride 25038-59-9, Polyethyleneterephthalate, analysis 31900-57-9, Polydimethylsiloxane
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
IT 150244-18-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(thiolation with; patterned deposition of antibody-**binding** proteins for optical diffraction-based **biosensors**)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 37 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:402097 HCAPLUS
DOCUMENT NUMBER: 133:40221
TITLE: Patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**
INVENTOR(S): Everhart, Dennis S.; Kaylor, Rosann M.; McGrath, Kevin
PATENT ASSIGNEE(S): Kimberly-Clark Worldwide, Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000034781	A2	20000615	WO 1999-US27671	19991122 <--
WO 2000034781	A3	20000817		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6221579	B1	20010424	US 1998-210016	19981211 <--
EP 1137942	A2	20011004	EP 1999-961755	19991122 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 759582	B2	20030417	AU 2000-18271	19991122 <--
US 2001004526	A1	20010621	US 2000-733204	20001208 <--
US 6573040	B2	20030603		
PRIORITY APPLN. INFO.:			US 1998-210016 A	19981211 <--
			WO 1999-US27671 W	19991122 <--

AB The present invention provides an inexpensive and sensitive system and method for detecting analytes present in a medium. The system comprises a diffraction enhancing element, such as functionalized microspheres, which are modified such that they are capable of **binding** with a target analyte. Addnl., the system comprises a polymer film, which may include a **metal** coating, upon which is printed a specific, predetd. pattern of analyte-specific receptors. Upon attachment of a target analyte to **select** areas of the polymer film, either directly or with the diffraction enhancing element, diffraction of transmitted and/or reflected light occurs via the phys. dimensions and defined, precise placement of the analyte. A diffraction image is produced which can be easily seen with the eye or, optionally, with a sensing device. Blue polystyrene particles were conjugated with monoclonal antibody. A gold/Mylar film was blocked with β-casein and then antibody was **immobilized** in a pattern on the surface. LH sample was mixed with the microparticles and then applied to the sensor. A nitrocellulose disk with a small hole in the center was used to wick away excess fluid and **unbound** microparticles. A point light source was transmitted through the hole and sensor to create a diffraction image on the other side.

IC ICM G01N033-53

CC 9-1 (Biochemical Methods)
Section cross-reference(s): 2, 3, 15

ST patterned functionalized microsphere optical diffraction **biosensor** ; LH immunosensor diffraction pattern

IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(A; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Nucleic acid hybridization
(DNA-DNA; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(E; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(G; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(M; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Autoimmune disease
Hepatitis
Human immunodeficiency virus 1
Human immunodeficiency virus 2
Microorganism
Rous sarcoma virus
Streptococcus group A
Streptococcus group B

(antigen of; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Polysulfones, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(aromatic; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Albumins, analysis
Polyoxyalkylenes, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as blocking material; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Latex
(as diffraction enhancing element; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Glass, analysis
Plastics, analysis
Polycarbonates, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(as diffraction enhancing element; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Flagella
Pilus
(bacterial; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Receptors
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(**conjugates**, with microsphere diffraction enhancer or with sensor; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group A; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group B; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group C; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group W-135; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Neisseria meningitidis
(group Y; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Antibodies
RL: ARG (Analytical reagent use); DEV (Device component use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(**immobilized**, thiolated; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Oligonucleotides
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(**immobilized**; patterned **binding** of functionalized

microspheres for optical diffraction-based **biosensors**)
IT Optical sensors
(immunol. **biosensors**, for LH; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT **Biosensors**
(immunol., optical, for LH; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT **Biosensors**
(immunosensors, optical, for LH; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(monoclonal, **conjugates**, with polystyrene particles; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT Bacteria (Eubacteria)
Biosensors
Candida albicans
Cellophane
Chelating agents
Drugs
Drugs of abuse
Environmental analysis
Escherichia coli
Films
Fungi
Microspheres
Optical diffraction
Scanning **electron** microscopy
Streptococcus pneumoniae
Surfactants
Virus
Yeast
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT **Allergens**
Carcinoembryonic antigen
Haptens
Rheumatoid factors
RL: ANT (Analyte); ANST (Analytical study)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT Antibodies
Antigens
Carbohydrates, analysis
Enzymes, analysis
Hormones, animal, analysis
Lipids, analysis
Nucleic acids
Polysaccharides, analysis
Proteins, general, analysis
RL: ANT (Analyte); ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT **Metals**, analysis
RL: ARG (Analytical reagent use); ARU (Analytical role, unclassified); DEV

(Device component use); ANST (Analytical study); USES (Uses)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Oligonucleotides
Receptors
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Ionomers
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Polyesters, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Polymers, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Polyamides, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(polyethylene copolymer; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Albumins, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(serum, as blocking material; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT **Antigens**
RL: ANT (Analyte); ANST (Analytical study)
(tumor-associated; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Haemophilus influenzae
(type b; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT Caseins, analysis
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(β-, as blocking material; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT 7704-34-9D, Sulfur, derivs., analysis 9002-89-5, Polyvinyl alcohol 25322-68-3
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as blocking material; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT 9003-53-6, Polystyrene 9004-34-6, Cellulose, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(as diffraction enhancing element; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

IT 274951-41-6D, thiolated, **immobilized**
RL: ARG (Analytical reagent use); DEV (Device component use); PRP

(Properties); ANST (Analytical study); USES (Uses)
(as probe; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT 9013-20-1, Streptavidin
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(particles coated with; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT 9003-53-6D, Polystyrene, **conjugates** with monoclonal antibody
RL: ARG (Analytical reagent use); ARU (Analytical role, unclassified); ANST (Analytical study); USES (Uses)
(particles; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT 9002-67-9, Luteinizing hormone
RL: ANT (Analyte); ANST (Analytical study)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT 274951-42-7D, biotinylated
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT 275358-38-8, SEKL 15 275358-42-4, SEKB 250
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT 7429-90-5, Aluminum, analysis 7439-89-6, Iron, analysis 7440-02-0, Nickel, analysis 7440-06-4, Platinum, analysis 7440-22-4, Silver, analysis 7440-47-3, Chromium, analysis 7440-50-8, Copper, analysis 7440-57-5, Gold, analysis 7440-67-7, Zirconium, analysis 9002-88-4 9003-07-0, Polypropylene 9003-56-9, Acrylonitrile-butadiene-styrene copolymer 9004-34-6D, Cellulose, compds., analysis 9004-35-7, Cellulose acetate 9004-36-8, Cellulose acetate butyrate 9004-48-2, Cellulose propionate 9004-57-3, Ethyl cellulose 9004-70-0, Nitrocellulose 9012-09-3, Cellulose triacetate 9016-80-2, Methyl pentene polymer 11118-57-3, Chromium oxide 24937-78-8 24968-79-4, Acrylonitrile-methyl acrylate copolymer 24981-14-4, Polyvinyl fluoride 25038-59-9, Polyethyleneterephthalate, analysis 31900-57-9, Polydimethylsiloxane 39403-39-9, Gold oxide
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)
IT 150244-18-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(thiolation with; patterned **binding** of functionalized microspheres for optical diffraction-based **biosensors**)

L44 ANSWER 38 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1999-12492 BIOTECHDS
TITLE: Biosensors used to detect analyte, e.g. chemical or biological contamination in garments, e.g. diapers; biosensor used to detect a yeast, fungus or bacterium, particularly to identify food contaminant or infection
AUTHOR: Everhart D S; Jones M L; Kaylor R M
PATENT ASSIGNEE: Kimberly-Clark-Worldwide
LOCATION: Neenah, WI, USA.
PATENT INFO: WO 9931486 **24 Jun 1999**
APPLICATION INFO: WO 1998-US26759 16 Dec 1998
PRIORITY INFO: US 1997-991644 **16 Dec 1997**
DOCUMENT TYPE: Patent
LANGUAGE: English

OTHER SOURCE: WPI: 1999-443884 [37]
AN 1999-12492 BIOTECHDS
AB A biosensor consisting of a polymer film, coated with a **metal**, and a patterned receptor layer printed on that film. The receptor layer contains a receptive material that **binds** an analyte. Also claimed is a means of detecting an analyte using the sensor, and a means of making the biosensors. The biosensor is used to detect chemical or biological contaminants in garments such as diapers, in foods and beverages and in biological samples, for diagnosis of e.g. infections. The **metal** is preferably gold, but may also be silver, nickel, platinum, iron, etc. The patterned layer is such that analyte **binding** results in light diffraction, forming a visible signal, particularly a hologram. The analyte detected is preferably a bacterium, yeast or fungus, but includes immunoglobulins, **antigens**, **antibodies**, enzymes, hormones, proteins, nucleic acids and drugs. The receptor material may be composed of **antigens**, **antibodies**, nucleotides, nucleic acids, enzymes, bacteria, viruses, polysaccharides, etc. The polymer layer is preferably composed of polyethylene terephthalate. (39pp)

L44 ANSWER 39 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:468663 HCAPLUS
DOCUMENT NUMBER: 131:113389
TITLE: Sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads
INVENTOR(S): Lee, Gil U.
PATENT ASSIGNEE(S): United States of America, Secretary of the Navy, USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9936577	A1	19990722	WO 1999-US1191		19990120 <--
W: AU, CA, JP, KR, MX					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 6180418	B1	20010130	US 1998-8782		19980120 <--
CA 2318581	AA	19990722	CA 1999-2318581		19990120 <--
AU 9925601	A1	19990802	AU 1999-25601		19990120 <--
AU 762294	B2	20030619			
EP 1049808	A1	20001108	EP 1999-905446		19990120 <--
R: CH, DE, FR, GB, IT, LI					
JP 2002509242	T2	20020326	JP 2000-540278		19990120 <--
PRIORITY APPLN. INFO.:			US 1998-8782	A	19980120 <--
			WO 1999-US1191	W	19990120 <--

AB A sensor for a **selected** target species has (1) a substrate which has been chemical modified by attachment of substrate modifiers; (2) one or more magnetically active beads which have been chemical modified by attachment of bead modifiers, where these bead modifiers will have a **binding** affinity for the substrate modifiers in the presence of the target species, and a measurably different **binding** affinity for the substrate modifiers in the absence of the target species; (3) an adjustable source of a magnetic field for exerting a force on the beads; and (4) an imaging system, for observing and counting beads **bound** to said substrate. In a preferred embodiment, the invention further has a

system for identifying clusters of beads, and for removing the effect of such clusters from measurements of the target analyte. As with other assays, the sensor relies on the ability of certain mols. to **bind** with specific target (analyte) mols. By coating the beads and the substrate with appropriate mols., the beads will (or will not) **bind** specifically to the substrate in the presence (or absence) of the target mol. When a magnetic field is applied to the substrate, the magnetic beads will be pulled away from the substrate. If the beads are specifically **bound** to the substrate, however, the beads will be retained on the substrate, indicating the presence (or absence) of the target species. Force discrimination assays were used to detect biotin and ovalbumin. The sensitivity of the ovalbumin assay was 100 pg/mL of ovalbumin.

IC ICM C12Q001-68
ICS G01N033-53; C07H019-00; C07H021-04

CC 9-1 (Biochemical Methods)

ST force discrimination assay sensor magnetic bead; specific **binding** assay **biosensor** magnetic bead; biotin force discrimination assay streptavidin superparamagnetic bead; ovalbumin force discrimination immunoassay antibody magnetic bead

IT **Immunoglobulins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(G, goat antibodies to, of rabbit, in indirect detection of ovalbumin using sandwich assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Magnetic field
(adjustable; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Magnets
(as adjustable magnetic field source; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Glycolipids
Hormones, animal, analysis
Peptides, analysis
RL: ANT (Analyte); ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(as bead modifier; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Chelating agents
(as substrate or bead modifier; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Antibodies
Haptens
Nucleic acids
Proteins, general, analysis
RL: ANT (Analyte); ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(as substrate or bead modifier; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Polyoxyalkylenes, reactions
RL: DEV (Device component use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(as water-soluble coating on substrate, substrate modifiers attachment to; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Magnetic particles

(beads, with **binding** affinity modifiers; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Molecular association
(between specific **binding** substances, determination of strength of; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Polyoxyalkylenes, biological studies
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(biotin **conjugates**, **immobilized**, in biotin detection by competitive assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Antibodies
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**conjugates**, with superparamagnetic beads, for ovalbumin detection by sandwich assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Ovalbumin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(detection of, by sandwich assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Force
(determination of, between specific **binding** substances; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Apparatus
(digital image acquisition and processing and counting systems; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Microscopes
Optical imaging devices
(for observing beads **bound** to substrate; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Antibodies
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**immobilized**, for ovalbumin detection by sandwich assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT CCD cameras
(in biotin detection by competitive assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT **Metals**, analysis
RL: ANT (Analyte); ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(ions, as bead modifier; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT Analysis
(magnetic; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT Adsorption
(region of substrate resistant to nonspecific; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT Immunoassay
(sandwich, in detection of ovalbumin using antibody-modified magnetic beads; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT Polymers, analysis
RL: ANT (Analyte); ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(**selective-binding**, as substrate or bead modifier; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT **Biosensors**
Computers
Sensors
(sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT Albumins, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(serum, biotinylated, detection of, by competitive assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT Paramagnetic materials
(superparamagnetic, streptavidin **conjugates**, in biotin detection by competitive assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT Microscopy
(video, in biotin detection by competitive assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT Coating materials
(water-soluble, polymer, modified, on substrate; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT 214051-31-7D, Dynal M 280, tosyl-activated
RL: RCT (Reactant); RACT (Reactant or reagent)
(anti-ovalbumin antibodies **conjugation** with; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT 25322-68-3
RL: DEV (Device component use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(as water-soluble coating on substrate, substrate modifiers attachment to; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT 58-85-5D, Biotin, bovine serum albumin **conjugates**
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(detection of, by competitive assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)
IT 9013-20-1D, Streptavidin, **conjugates** with superparamagnetic beads

RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(in biotin detection by competitive assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

IT 25322-68-3DP, Polyethylene glycol, biotin **conjugates**, **immobilized**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(in biotin detection by competitive assay; sensor for specific **binding** force discrimination assay using modified substrate and magnetic beads)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 40 OF 48 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-456895 [38] WPIX
CROSS REFERENCE: 1997-528795 [49]; 1998-132317 [13]; 1999-262677 [22]; 1999-443010 [37]; 1999-458103 [38]; 2000-327693 [28]; 2002-225857 [28]; 2004-398954 [37]
DOC. NO. NON-CPI: N1999-341658
DOC. NO. CPI: C1999-134004
TITLE: Ionically attaching biomolecules to the surfaces of medical devices.
DERWENT CLASS: A14 A31 A35 A96 B04 B05 B07 C07 D16 D22 G02 S03
INVENTOR(S): KEOGH, J R
PATENT ASSIGNEE(S): (MEDT) MEDTRONIC INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5928916	A	19990727	(199938)*		7

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 5928916	A	CIP of	US 1996-635187	19960425
		CIP of	US 1996-694535	19960809
		CIP of	US 1997-984922	19971204
		CIP of	US 1997-1994	19971231
			US 1998-10906	19980122

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 5928916	A	CIP of	US 5728420
		CIP of	US 5821343

PRIORITY APPLN. INFO: US 1998-10906 19980122; US 1996-635187 19960425; US 1996-694535 19960809; US 1997-984922 19971204; US 1997-1994 19971231
AN 1999-456895 [38] WPIX

CR 1997-528795 [49]; 1998-132317 [13]; 1999-262677 [22]; 1999-443010 [37]; 1999-458103 [38]; 2000-327693 [28]; 2002-225857 [28]; 2004-398954 [37]

AB US 5928916 A UPAB: 20040611

NOVELTY - The ionic attachment of biomolecules to the surfaces of medical implants, using positively charged guanidino moieties, is new. This process is used to form coatings on the surfaces of medical devices (Method (I)) to impart improved biocompatability characteristics and make the surfaces suitable for contact with bodily tissues and fluids.

DETAILED DESCRIPTION - A method (I) for forming coatings on the surfaces of medical devices to impart improved biocompatability characteristics and make the surfaces suitable for contact with bodily tissues and fluids both in vivo and ex vivo. (I) comprises:

(i) providing a medical device (X) which has a surface comprising a biomaterial and a positively charged guanidino moiety (a);

(ii) providing a biomolecule comprising a negatively charged moiety (b); and

(iii) combining (a) and (b) to form an ionic bond which **immobilizes** the biomolecule, forming a coating on the surface of (X).

USE - Method (I) may be used to modify the surfaces of medical devices, such as implants, so that they have improved biocompatability characteristics and are suitable for contact with body fluids and tissues both in vivo and ex vivo. Substrates which may be modified in this way include **metals** (e.g. titanium, aluminum oxide and stainless steel), elgiloy, haynes 25, stellite, pyrolytic carbon, silver carbon, glassy carbon, polymers (e.g. polypropylene, polyvinylchlorides and polystyrene), rubber, minerals, ceramics (e.g. hydroxapatite), human or animal protein or tissue (e.g. bone, skin and collagen), other organic materials (e.g. wood and compressed carbon) and other materials (e.g. glass).

The modified substances may then be used to form a wide variety of products with any shape (e.g. flat sheets and tubes), such as vascular grafts, ultrafiltration membranes, catheters, prosthetic heart valves, cardiac pacemaker leads, lens for eyes, biosensors, dental devices, blood bags and intraaortic balloons.

ADVANTAGE - The products modified in this way have improved biocompatability characteristics and reduce the risk of postoperative infections caused by microbes colonizing implants. Also, these products do not absorb bodily fluids and tissues, which may build up in the surface layer of the implant and affect its interaction with the patient's physiology. In particular, heparin may be **bound** to the surface of the biomaterial to prevent coagulation of blood within its surface. Additionally, the ionic reaction between the guanidino and the negatively charged biomolecule, as well as being reversible, does not cause changes to the structure and function of the biomolecule so it maintains its activity.

Dwg.0/0

L44 ANSWER 41 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1998-10354 BIOTECHDS
TITLE: Apparatus for electrochemically detecting **binding** of **binding** pair members;
specific biological **binding** pair electrochemical **binding** detection for use in screening assay for detection of **binding** inhibition for e.g. drug development, biochemical analysis, etc.
AUTHOR: Fowlkes D M; Thorp H H
PATENT ASSIGNEE: Univ.North-Carolina; Novalon-Pharmaceutical
LOCATION: Chapel Hill, NC, USA.
PATENT INFO: WO 9835232 **13 Aug 1998**

APPLICATION INFO: WO 1998-US2440 6 Feb 1998
PRIORITY INFO: US 1997-59049 **16 Sep 1997**; US 1997-36919 6 Feb 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-467163 [40]
AN 1998-10354 BIOTECHDS
AB An apparatus used in an electrochemical assay to detect **binding** between members of a biological **binding** pair (BBP) is claimed. It consists of a 1st electrode coated with a porous hydrophilic polymer layer on which one half of the BBP is **immobilised.** The apparatus also contains a 2nd electrode and 3rd electrode, both made of conducting **metal.** A reaction chamber contains an electrolyte solution in contact with all of the electrodes. The solution contains an electrochemical mediator capable of participating in a redox reaction with the electrodes, and a 2nd member of the BBP, optionally **bound** to a catalyst. The mediator can alternatively be **immobilized** to the 1st electrode. The preferred apparatus uses cyclic voltammetry or chronoamperometry, and consists of multiple electrode pairs, and reaction chambers. The 1st part of the BBP is a receptor protein, an **antibody** protein, or a 1st protein. The 2nd part is a ligand specific for the receptor, an **antigen** or a 2nd protein, and is ruthenium or osmium labeled. A catalyst **bound** to the 2nd BBP is an enzyme, e.g. horseradish (Armoracia rusticana) peroxidase (EC-1.11.1.7). (104pp)

L44 ANSWER 42 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1997-06861 BIOTECHDS
TITLE: New molecules which may be used in biosensors; potential biosensor construction by biological **binding** partner **immobilization** for e.g. DNA or RNA hybridization
AUTHOR: Bamdad C C; Sigal G B; Strominger J L; Whitesides G M
PATENT ASSIGNEE: Univ.Harvard
LOCATION: Cambridge, MA, USA.
PATENT INFO: US 5620850 **15 Apr 1997**
APPLICATION INFO: US 1994-312388 26 Sep 1994
PRIORITY INFO: US 1994-312388 **26 Sep 1994**
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1997-235174 [21]
AN 1997-06861 BIOTECHDS
AB A species of formula X-R-Ch-M is claimed, where X = a functional group and R = a spacer moiety that, together promote formation of a self-assembled monolayer on a surface, Ch = a chelating agent (I) that coordinates a **metal** ion, and M = a **metal** ion coordinated to (I), where M also is coordinated to a biological **binding** partner of a biological molecule (BM) via coordination sites not filled by (I) or includes coordination sites not filled by (I) that, upon exposure to a polyamino acid tag, are able to become coordinated by the polyamino acid tag. (I) is a quadradentate agent, especially nitrilotriacetic acid. X adheres to a gold surface and X-R-Ch = a thiol-linked nitrilotriacetic acid chelate. Also claimed is X-R-Ch-M-BP, where BP = a BM coordinated to the **metal** ion. The materials can be used to capture BMs, especially for biosensors, e.g. for determination of **binding** partners of nucleic acid. The materials facilitate surface **immobilization** BM **binding** partners. The BMs may be enzymes and substrate or inhibitor or coenzyme, hormones and receptors, receptor and virus, etc. Biosensor sensitivity is high and non-specific **binding** is minimal. (19pp)

L44 ANSWER 43 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1996-08007 BIOTECHDS
TITLE: Sensor for detecting superoxide anion comprises hydrogen peroxide indicating electrode;
tissue electrode or enzyme electrode biosensor with lymphocyte, macrophage, leukocyte or epithelium cells, xanthine-oxidase, lipoxygenase or NADH-oxidase, and superoxide-dismutase
AUTHOR: Scheller F; Bier F
PATENT ASSIGNEE: Scheller F
LOCATION: Zepernick, Germany.
PATENT INFO: DE 4438087 **2 May 1996**
APPLICATION INFO: DE 1994-4438087 25 Oct 1994
PRIORITY INFO: DE 1994-4438087 **25 Oct 1994**
DOCUMENT TYPE: Patent
LANGUAGE: German
OTHER SOURCE: WPI: 1996-222722 [23]
AN 1996-08007 BIOTECHDS
AB A new tissue electrode or enzyme electrode biosensor for superoxide (SO) detection contains an SO-producing agent or measurement solution in direct contact with a gas-permeable membrane and an amperometric or potentiometric hydrogen peroxide-indicating electrode, coated with a compound which causes SO disproportionation. The SO-producing agent may be a lymphocyte, macrophage, leukocyte, epithelium cell, xanthine-oxidase (EC-1.1.3.22), lipoxygenase (EC-1.13.11.12), NADH-oxidase, or an **antibody** or **antigen** coupled to these enzymes. The disproportionation reagent is preferably superoxide-dismutase (EC-1.15.1.1) or a low-mol.weight **metal** complex. The biosensor may be used to detect or determine living cells and biological macromolecules, and may be miniaturized for use as a probe to locate SO sources in organisms and cells. Interfering effects of other substances (e.g. H2O2 or ascorbic acid) are completely eliminated. SO can pass through the membrane and degrade at the electrode to H2O2, to generate a signal proportional to SO concentration, and O2. Addition of a scavenger enzyme is not necessary. (3pp)

L44 ANSWER 44 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1994-04360 BIOTECHDS
TITLE: New modified **antibody** with attached thiol containing residue;
monoclonal **antibody** modification with thiol-containing residue covalent attachment to Fc followed by **immobilization** to solid adsorbent; application as immunosensor
PATENT ASSIGNEE: CSIRO
PATENT INFO: WO 9403496 **17 Feb 1994**
APPLICATION INFO: WO 1993-AU386 30 Jul 1993
PRIORITY INFO: AU 1992-3809 **30 Jul 1992**; AU 1992-3808 30 Jul 1992
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1994-065611 [08]
AN 1994-04360 BIOTECHDS
AB A new modified **antibody** (Ab), or its fragments or conjugates, has at least 1 thiol-containing residue (A) covalently attached to its Fc tail. Also new are substrates having Ab **immobilized** on them in the correct orientation for **binding** an **antigen.**
Preferably, (A) are of the formula -CH=N-NH-CO-R-S-R' or -CH=N-NH-R-S-R', where R' = H or R''; R and R'' = optionally substituted aliphatic, aromatic or alicyclic group; oligo(ethylene oxide) chain, or a mono- or oligosaccharide residue. The Abs are monoclonal or polyclonal derived

from a human or other animal. Substrates carrying the Ab are useful as biomaterials or biosensors, able to **bind antigen** with high affinity and specificity. Particularly they **bind** proteins (especially enzymes or other Abs) and/or cells which then form a further layer on the surface. Substrates include polymers, **metals**, ceramics, etc., optionally formulated on a film (especially golds for biosensor applications). Attachment via Fc ensures that the **antigen-binding** fragments are orientated away from the surface, improving **antigen binding.** (26pp)

L44 ANSWER 45 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1992-10213 BIOTECHDS
TITLE: Substrate coated with pattern of orientated mutant proteins; enzyme, **antibody**, **antigen**, heme protein engineering; mutant protein with preferential **binding** site **immobilization** on support or adsorbent may be used as an electrical or optical biosensor
PATENT ASSIGNEE: Univ.Illinois; Biotech.Res.Develop.
PATENT INFO: WO 9208788 **29 May 1992**
APPLICATION INFO: WO 1991-US8595 18 Nov 1991
PRIORITY INFO: US 1990-615046 **19 Nov 1990**
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1992-200173 [24]
AN 1992-10213 BIOTECHDS
AB A substrate (A) is coated with a pattern of mutated proteins (I), each of which includes a marker (M) and can be orientated on a substrate provided with functional groups. (I) are variants of a randomly-positioning protein (Ia) with mutations at one or more selected positions in the amino acid (AA) position in the (Ia) sequence to generate a preferential **binding** site (PBS) having a reactive AA able to **bind** to the specified functional groups. The PBS and M have a predetermined spatial relationship, while the M groups have a similar relationship with respect to the substrate and M on adjacent (I). More specifically, (I) are mutant forms of heme proteins e.g. cytochrome-a, -b, or -c, or myoglobin. In a preferred system, (Ia) is a **metallo** protein, enzyme, **antibody** or **antigen** with AA mutations on the molecule surface. Suitable (A) are **metals**, silica and **metal** oxides. The coated substrates are useful in electrical and optical devices, e.g. phase gratings, spatial light modulators, variable integrated optical waveplates, integrated optical sensors, etc. (53pp)

L44 ANSWER 46 OF 48 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:648170 HCAPLUS
DOCUMENT NUMBER: 117:248170
TITLE: Separation method, sensor, and kit for specific **binding** assay
INVENTOR(S): Abuknesha, Ramadan Arbi; Byfield, Mark Philip
PATENT ASSIGNEE(S): GEC-Marconi Ltd., UK
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9216838	A1	19921001	WO 1992-GB506	19920320 <--

W: JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE
GB 2255637 A1 19921111 GB 1992-6082 19920320 <--
GB 2255637 B2 19951115
EP 640216 A1 19950301 EP 1992-907150 19920320 <--
EP 640216 B1 20021002
R: AT, CH, DE, FR, IT, LI, NL
AT 225512 E 20021015 AT 1992-907150 19920320 <--
CA 2106339 AA 19950317 CA 1993-2106339 19930916 <--
PRIORITY APPLN. INFO.: GB 1991-5921 A 19910320 <--
GB 1991-27346 A 19911224 <--
WO 1992-GB506 W 19920320 <--

AB A separation method for use in immunoassays etc. involves use of an auxiliary species on a support material and a **binding** species capable of (1) **binding** to the auxiliary species and (2) being linked with a primary species (analyte, ligand, antibody) by a specific or nonspecific linkage. The support may be glass, quartz, or an **electrode.** The auxiliary species may be an antigenic or nonantigenic ligand, e.g. 2,4-DNP, fluorescein, digoxin, coumarin, or biotin or an oligomer or polymer thereof, and the **binding** species may be an antibody to the auxiliary species or avidin. Sensors and assay kits having the above construction for **binding** an analyte, for use with labeled antibodies, are claimed. Thus, a competitive immunoassay for 17β-estradiol used an ovalbumin conjugate of 7-amino-4-methylcoumarin-3-propionic acid (I) adsorbed on a microtiter plate as the auxiliary species, a conjugate of an anti-I antibody with 17β-estradiol 3-(O-carboxymethyl) ether (II) as **binding** species linked to a primary species, a rabbit anti-II antibody as primary antibody, and a donkey anti-rabbit **Ig** antibody conjugated with peroxidase as secondary antibody.

IC G01N033-537; G01N033-543; G01N027-327; G01N033-50; G01N033-58; G01N033-18; G01N033-24; G01M033-04
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 2, 79, 80
ST immunoassay **biosensor** kit; estradiol immunoassay; EIA estradiol

IT Chelating agents
(analyte **binding** by, in immunoassay, auxiliary ligand in relation to)

IT **Antigens**
RL: ANST (Analytical study)
(as auxiliary ligands, in immunoassay)

IT **Electrodes**
Glass, oxide
Polyamides, uses
RL: ANST (Analytical study)
(auxiliary ligand **immobilization** on, in immunoassay)

IT Ligands
RL: ANST (Analytical study)
(auxiliary, in specific **binding** assay)

IT Avidins
RL: ANST (Analytical study)
(biotin auxiliary ligand **binding** by, in immunoassay)

IT Analysis
(by specific **binding** assay, auxiliary ligands in, kits and sensors in relation to)

IT Albumins, analysis
Coordination compounds
Hormones
Metals, analysis
Steroids, analysis

Toxins
RL: ANT (Analyte); ANST (Analytical study)
(determination of, by immunoassay, auxiliary ligand in relation to)
IT **Biosensors**
(for specific **binding** assay, auxiliary ligands in relation to)
IT Adsorption
(of auxiliary ligand to **binding** ligand, in specific **binding** assay)
IT **Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(G, determination of, by immunoassay, auxiliary ligand in relation to)
IT Ovalbumins
RL: ANST (Analytical study)
(**conjugates**, with auxiliary ligand, in estradiol determination by immunoassay)
IT Trace elements, analysis
RL: ANT (Analyte); ANST (Analytical study)
(**metals**, determination of, by immunoassay, auxiliary ligand in relation to)
IT Particles
(micro-, ferrous oxide-containing, auxiliary ligand **immobilization** on, in immunoassay)
IT 106145-38-4 106145-38-4D, derivs. 60-00-4, EDTA, biological studies 67-43-6, DTPA 70-51-9, Deferoxamine 148-24-3, 8-Quinolinol, biological studies 148-24-3D, 8-Quinolinol, derivs. 482-54-2
RL: ANST (Analytical study)
(analyte **binding** by, in immunoassay, auxiliary ligand in relation to)
IT 113721-82-7D, ovalbumin **conjugates**
RL: ANST (Analytical study)
(as auxiliary ligand, in estradiol determination by immunoassay)
IT 7631-86-9D, Silica, derivs. 9003-53-6, Polystyrene 14808-60-7, Quartz, uses
RL: ANST (Analytical study)
(auxiliary ligand **immobilization** on, in immunoassay)
IT 9004-54-0, Dextran, biological studies
RL: BIOL (Biological study)
(crosslinked, auxiliary ligand **immobilization** on, in immunoassay)
IT 58-85-5, Biotin 71-63-6, Digitoxin 91-64-5, Coumarin 2321-07-5, Fluorescein 51-28-5, 2,4-Dinitrophenol, uses
RL: ANST (Analytical study)
(**immobilized**, as auxiliary ligand in immunoassay)
IT 41164-36-7D, **conjugate** with antibody to auxiliary ligand
RL: ANST (Analytical study)
(in estradiol determination by immunoassay)
IT 1345-25-1, Ferrous oxide, biological studies
RL: BIOL (Biological study)
(microparticles containing, auxiliary ligand **immobilization** on, in immunoassay)

L44 ANSWER 47 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1992-03152 BIOTECHDS
TITLE: Biosensor with surface electrodes formed photolithographically;
on piezoelectric substrate, uses surface skimming bulk waves and has bio-sensitive surface protein
PATENT ASSIGNEE: GEC-Marconi
PATENT INFO: EP 459613 **4 Dec 1991**

APPLICATION INFO: EP 1991-303314 15 Apr 1991
PRIORITY INFO: GB 1990-12247 **1 Jun 1990**
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1991-355877 [49]
AN 1992-03152 BIOTECHDS
AB A new biosensor comprises a piezoelectric support with electrodes on its surface. The support is a single crystal with the electrodes photolithographically deposited as elongated regions of **metallization** (ERMs) transverse to the direction of wave propagation. The **metallized** regions have their width and spacing of the same order. Protein is **immobilized** on the surface of the support. Mass loading of the surface of the crystal may be increased by the formation of a grating including the ERMs. This may include additional **metallic** fingers interdigited between the ERMs. There may also be troughs formed in the surface of the crystal between the ERMs. The biosensor may be used for detecting **antigens** using specific **antibody-antigen binding.** The test may be carried out in a liquid environment. When immersed in a liquid phase test solution, the biosensor produces a surface skimming bulk acoustic wave having a liquid penetration of less than 500 A. (7pp)

L44 ANSWER 48 OF 48 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 1987-06614 BIOTECHDS
TITLE: Oxygen electrode and oxygen sensor; containing **immobilized** enzyme, microorganism or **antibody**
PATENT ASSIGNEE: Fujitsu
PATENT INFO: JP 62039754 **20 Feb 1987**
APPLICATION INFO: JP 1985-179276 16 Aug 1985
PRIORITY INFO: JP 1985-179276 **16 Aug 1985**
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 1987-089978 [13]
AN 1987-06614 BIOTECHDS
AB An oxygen electrode for measuring the dissolved oxygen concentration in a solution has an anode, cathode and electrolyte solution. The electrode comprises a closed cylindrical container consisting of 2 halves cut along the longitudinal direction, which is filled with the electrolyte solution. The inner surface of 1 half is coated with a **metal** as the anode, and in the wall of the other half at least 1 opening is provided across which a **metal** which functions as the cathode is provided to partially cover the opening. A membrane of oxygen-permeable material covers the opening over this **metal.** An enzyme, **antigen**, **antibody** or microorganism is **immobilized** on the membrane of oxygen-permeable material to form the oxygen sensor. (3pp)

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